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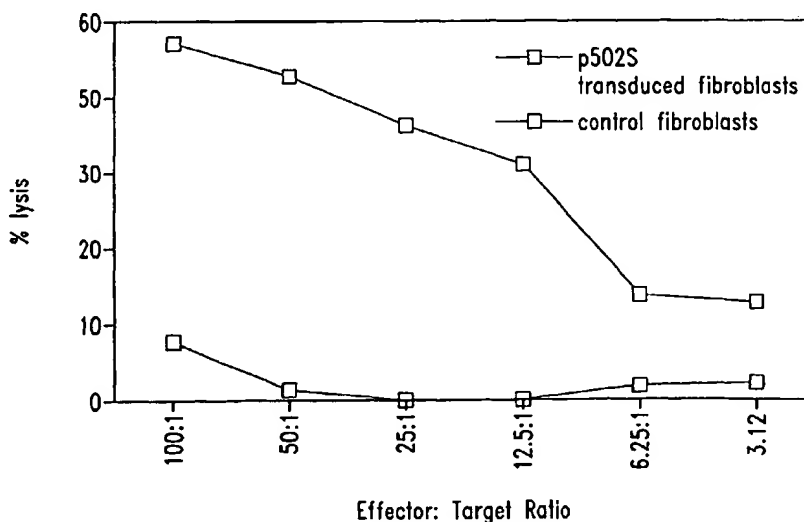
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(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.



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## COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

### 5 TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for  
10 prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

### BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress  
15 inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but  
20 these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate  
25 with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

### 30 SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the



diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-550.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier. In certain embodiments, the present invention provides monoclonal antibodies that specifically bind to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 522 and 541-550, together with monoclonal antibodies comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

5           Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

10           Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

15           Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that  
20           specifically react with a prostate-specific protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described  
25           above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time  
30           sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

10 Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

15

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

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The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain

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embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that  
5 hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b)  
10 detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as  
15 monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed  
20 herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

#### BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The  
25 percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure  
30 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

5 Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

10 Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

20 Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

25 Figure 11 shows the results of an ELISA assay of antibody specificity to P501S peptides.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16

30 SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9

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SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296

SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280

SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)

5

SEQ ID NO: 108 is the predicted amino acid sequence for F1-12

SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17

SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as

10 P503S)

SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also referred to as P501S)

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15 SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-4738  
SEQ ID NO: 181 is the determined extended cDNA sequence for 1G-4741  
SEQ ID NO: 182 is the determined extended cDNA sequence for 1G-4744  
SEQ ID NO: 183 is the determined extended cDNA sequence for 1H-4774  
SEQ ID NO: 184 is the determined extended cDNA sequence for 1H-4781  
20 SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-4785  
SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-4787  
SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-4796  
SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-4807  
SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810  
25 SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811  
SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-4876  
SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-4884  
SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-4896  
SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-4761  
30 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762  
SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766  
SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770

- SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
- SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772
- SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309
- SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278
- 5 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288
- SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283
- SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304
- SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296
- SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280
- 10 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
- SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
- SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
- SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
- SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
- 15 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd
- SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev
- SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd
- SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev
- SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd
- 20 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev
- SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd
- SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev
- SEQ ID NO: 220 is the determined cDNA sequence for 8-h11 rev
- SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd
- 25 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev
- SEQ ID NO: 223 is the determined cDNA sequence for P509S
- SEQ ID NO: 224 is the determined cDNA sequence for P510S
- SEQ ID NO: 225 is the determined cDNA sequence for P703DE5
- SEQ ID NO: 226 is the determined cDNA sequence for 9-A11
- 30 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6
- SEQ ID NO: 228 is the determined cDNA sequence for 8-H7
- SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13

SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14  
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23  
SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24  
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25  
5 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30  
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34  
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35  
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36  
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38  
10 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39  
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40  
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41  
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42  
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45  
15 SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46  
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51  
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56  
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64  
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65  
20 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67  
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76  
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84  
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85  
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86  
25 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87  
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88  
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1  
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2  
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2  
30 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1  
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2  
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3

- SEQ ID NO: 262 is the determined cDNA sequence for JP1A4  
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5  
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6  
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6  
5 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5  
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6  
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8  
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7  
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9  
10 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10  
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9  
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12  
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12  
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11  
15 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11  
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12  
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12  
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12  
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2  
20 SEQ ID NO: 281 is the determined cDNA sequence for JP8H1  
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2  
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3  
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4  
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3  
25 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4  
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6  
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6  
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5  
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8  
30 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7  
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7  
SEQ ID NO: 293 is the determined cDNA sequence for P8D8

- SEQ ID NO: 294 is the determined cDNA sequence for JP8E7  
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8  
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8  
SEQ ID NO: 297 is the determined cDNA sequence for JP8B10  
5 SEQ ID NO: 298 is the determined cDNA sequence for JP8C10  
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9  
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10  
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9  
SEQ ID NO: 302 is the determined cDNA sequence for JP8H9  
10 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12  
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11  
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12  
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12  
SEQ ID NO: 307 is the determined cDNA sequence for P711P  
15 SEQ ID NO: 308 is the determined cDNA sequence for P712P  
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23  
SEQ ID NO: 310 is the determined cDNA sequence for P774P  
SEQ ID NO: 311 is the determined cDNA sequence for P775P  
SEQ ID NO: 312 is the determined cDNA sequence for P715P  
20 SEQ ID NO: 313 is the determined cDNA sequence for P710P  
SEQ ID NO: 314 is the determined cDNA sequence for P767P  
SEQ ID NO: 315 is the determined cDNA sequence for P768P  
SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes  
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5  
25 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5  
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26  
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26  
SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23  
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23  
30 SEQ ID NO: 332 is the determined full length cDNA sequence for P509S  
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)  
SEQ ID NO: 334 is the determined cDNA sequence for P714P

- SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)
- SEQ ID NO: 336 is the predicted amino acid sequence for P705P
- SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10
- SEQ ID NO: 338 is the amino acid sequence of the peptide p5
- 5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S
- SEQ ID NO: 340 is the determined cDNA sequence for P778P
- SEQ ID NO: 341 is the determined cDNA sequence for P786P
- SEQ ID NO: 342 is the determined cDNA sequence for P789P
- SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo
- 10 sapiens MM46 mRNA
- SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
- SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin
- 15 SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)
- SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)
- SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo
- 20 sapiens phosphoglucomutase-related protein (PGMRP)
- SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40
- SEQ ID NO: 350 is the determined cDNA sequence for P777P
- SEQ ID NO: 351 is the determined cDNA sequence for P779P
- 25 SEQ ID NO: 352 is the determined cDNA sequence for P790P
- SEQ ID NO: 353 is the determined cDNA sequence for P784P
- SEQ ID NO: 354 is the determined cDNA sequence for P776P
- SEQ ID NO: 355 is the determined cDNA sequence for P780P
- SEQ ID NO: 356 is the determined cDNA sequence for P544S
- 30 SEQ ID NO: 357 is the determined cDNA sequence for P745S
- SEQ ID NO: 358 is the determined cDNA sequence for P782P
- SEQ ID NO: 359 is the determined cDNA sequence for P783P



- SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984
- SEQ ID NO: 361 is the determined cDNA sequence for P787P
- SEQ ID NO: 362 is the determined cDNA sequence for P788P
- SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994
- 5 SEQ ID NO: 364 is the determined cDNA sequence for P781P
- SEQ ID NO: 365 is the determined cDNA sequence for P785P
- SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.
- SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.
- 10 SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.
- SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.
- SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.
- 15 SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.
- SEQ ID NO: 381 is the determined cDNA sequence for B716P.
- SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.
- 20 SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
- SEQ ID NO: 384 is the cDNA sequence for P1000C.
- SEQ ID NO: 385 is the cDNA sequence for CGI-82.
- SEQ ID NO: 386 is the cDNA sequence for 23320.
- SEQ ID NO: 387 is the cDNA sequence for CGI-69.
- 25 SEQ ID NO: 388 is the cDNA sequence for L-iditol-2-dehydrogenase.
- SEQ ID NO: 389 is the cDNA sequence for 23379.
- SEQ ID NO: 390 is the cDNA sequence for 23381.
- SEQ ID NO: 391 is the cDNA sequence for KIAA0122.
- SEQ ID NO: 392 is the cDNA sequence for 23399.
- 30 SEQ ID NO: 393 is the cDNA sequence for a previously identified gene.
- SEQ ID NO: 394 is the cDNA sequence for HCLBP.
- SEQ ID NO: 395 is the cDNA sequence for transglutaminase.

- SEQ ID NO:396 is the cDNA sequence for a previously identified gene.
- SEQ ID NO:397 is the cDNA sequence for PAP.
- SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.
- SEQ ID NO:399 is the cDNA sequence for hTGR.
- 5 SEQ ID NO:400 is the cDNA sequence for KIAA0295.
- SEQ ID NO:401 is the cDNA sequence for 22545.
- SEQ ID NO:402 is the cDNA sequence for 22547.
- SEQ ID NO:403 is the cDNA sequence for 22548.
- SEQ ID NO:404 is the cDNA sequence for 22550.
- 10 SEQ ID NO:405 is the cDNA sequence for 22551.
- SEQ ID NO:406 is the cDNA sequence for 22552.
- SEQ ID NO:407 is the cDNA sequence for 22553.
- SEQ ID NO:408 is the cDNA sequence for 22558.
- SEQ ID NO:409 is the cDNA sequence for 22562.
- 15 SEQ ID NO:410 is the cDNA sequence for 22565.
- SEQ ID NO:411 is the cDNA sequence for 22567.
- SEQ ID NO:412 is the cDNA sequence for 22568.
- SEQ ID NO:413 is the cDNA sequence for 22570.
- SEQ ID NO:414 is the cDNA sequence for 22571.
- 20 SEQ ID NO:415 is the cDNA sequence for 22572.
- SEQ ID NO:416 is the cDNA sequence for 22573.
- SEQ ID NO:417 is the cDNA sequence for 22573.
- SEQ ID NO:418 is the cDNA sequence for 22575.
- SEQ ID NO:419 is the cDNA sequence for 22580.
- 25 SEQ ID NO:420 is the cDNA sequence for 22581.
- SEQ ID NO:421 is the cDNA sequence for 22582.
- SEQ ID NO:422 is the cDNA sequence for 22583.
- SEQ ID NO:423 is the cDNA sequence for 22584.
- SEQ ID NO:424 is the cDNA sequence for 22585.
- 30 SEQ ID NO:425 is the cDNA sequence for 22586.
- SEQ ID NO:426 is the cDNA sequence for 22587.
- SEQ ID NO:427 is the cDNA sequence for 22588.

- SEQ ID NO:428 is the cDNA sequence for 22589.  
SEQ ID NO:429 is the cDNA sequence for 22590.  
SEQ ID NO:430 is the cDNA sequence for 22591.  
SEQ ID NO:431 is the cDNA sequence for 22592.  
5 SEQ ID NO:432 is the cDNA sequence for 22593.  
SEQ ID NO:433 is the cDNA sequence for 22594.  
SEQ ID NO:434 is the cDNA sequence for 22595.  
SEQ ID NO:435 is the cDNA sequence for 22596.  
SEQ ID NO:436 is the cDNA sequence for 22847.  
10 SEQ ID NO:437 is the cDNA sequence for 22848.  
SEQ ID NO:438 is the cDNA sequence for 22849.  
SEQ ID NO:439 is the cDNA sequence for 22851.  
SEQ ID NO:440 is the cDNA sequence for 22852.  
SEQ ID NO:441 is the cDNA sequence for 22853.  
15 SEQ ID NO:442 is the cDNA sequence for 22854.  
SEQ ID NO:443 is the cDNA sequence for 22855.  
SEQ ID NO:444 is the cDNA sequence for 22856.  
SEQ ID NO:445 is the cDNA sequence for 22857.  
SEQ ID NO:446 is the cDNA sequence for 23601.  
20 SEQ ID NO:447 is the cDNA sequence for 23602.  
SEQ ID NO:448 is the cDNA sequence for 23605.  
SEQ ID NO:449 is the cDNA sequence for 23606.  
SEQ ID NO:450 is the cDNA sequence for 23612.  
SEQ ID NO:451 is the cDNA sequence for 23614.  
25 SEQ ID NO:452 is the cDNA sequence for 23618.  
SEQ ID NO:453 is the cDNA sequence for 23622.  
SEQ ID NO:454 is the cDNA sequence for folate hydrolase.  
SEQ ID NO:455 is the cDNA sequence for LIM protein.  
SEQ ID NO:456 is the cDNA sequence for a known gene.  
30 SEQ ID NO:457 is the cDNA sequence for a known gene.  
SEQ ID NO:458 is the cDNA sequence for a previously identified gene.  
SEQ ID NO:459 is the cDNA sequence for 23045.

SEQ ID NO:460 is the cDNA sequence for 23032.

SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NO:462-467 are cDNA sequences for known genes.

SEQ ID NO:468-471 are cDNA sequences for P710P.

5 SEQ ID NO:472 is a cDNA sequence for P1001C.

SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).

SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).

10 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).

SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).

SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO:  
15 474.

SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.

20 SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO:  
25 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

30 SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

5 SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

10 SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

15 SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P. SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

SEQ ID NO: 527 is the predicted amino acid sequence for P790P.

SEQ ID NO: 528 & 529 are PCR primers.

20 SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.

SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.

25 SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.

SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.

SEQ ID NO: 539 is the peptide P501S-370.

30 SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-550 are epitopes of P501S.

SEQ ID NO: 551 corresponds to amino acids 543-553 of P501S.

## DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate-specific protein or a variant thereof. A "prostate-specific protein" is a protein that is expressed in normal prostate and/or prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a non-prostate normal tissue, as determined using a representative assay provided herein. Certain prostate-specific proteins are proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate-specific proteins. Sequences of polynucleotides encoding certain prostate-specific proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Sequences of polypeptides comprising at least a portion of a prostate-specific protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

## PROSTATE-SPECIFIC PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate-specific protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred

polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate-specific protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate-specific protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate-specific protein or a portion thereof. The term "variants" also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices

for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenesis pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the “percentage of sequence identity” is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate-specific protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such



as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate-specific than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate-specific cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into

a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments; using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate-specific protein are provided in SEQ ID NO:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536.

Isolation of these polynucleotides is described below. Each of these prostate-specific proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis.

5 Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (*see* Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate-specific protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain  
10 portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (*e.g.*, by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate-specific polypeptide, and administering the transfected cells to the patient).

15 A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a protein. Antisense technology can be used to control gene expression  
20 through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (*see* Gee et al., *In* Huber and Carr, *Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (*e.g.*, promoter, enhancer or transcription initiation site), and block transcription of  
25 the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30  
30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'

ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

5           Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector  
10 will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

          Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for  
15 therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). The polynucleotides may also be administered as naked plasmid vectors.  
20 Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary  
25 skill in the art.

          Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane  
30 vesicle). The preparation and use of such systems is well known in the art.

## PROSTATE-SPECIFIC POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by normal prostate and/or prostate tumor cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the

immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example,  $^{125}\text{I}$ -labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate-specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino

acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known prostate-specific protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner),

preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are



an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent  
5 adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release  
10 formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix  
15 and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical  
20 compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the  
25 antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or  
30 progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy,

located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

5 Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 10 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The 15 lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as 20 LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been 25 exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion 30 incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its

original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector  
5 that is not a part of the natural environment:

#### BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an  
10 antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding  
15 constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about  $10^3$  L/mol. The binding constant may be determined using methods well known in the art.

20 Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals  
25 without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the  
30 above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Most preferably, antibodies employed in the inventive methods have the ability to induce lysis of tumor cells by activation of complement and mediation of antibody-dependent cellular cytotoxicity (ADCC). Antibodies of different classes and subclasses differ in these properties. For example, mouse antibodies of the IgG2a and IgG3 classes are capable of activating serum complement upon binding to target cells which express the antigen against which the antibodies were raised, and can mediate ADCC.

Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells

and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are  
5 selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse.  
10 Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

The preparation of mouse and rabbit monoclonal antibodies that specifically bind to  
15 polypeptides of the present invention is described in detail below. However, the antibodies of the present invention are not limited to those derived from mice. Human antibodies may also be employed in the inventive methods and may prove to be preferable. Such antibodies can be obtained using human hybridomas as described by Cote *et al.* (Monoclonal Antibodies and Cancer Therapy, Alan R. Lisa, p. 77, 1985). The present invention also encompasses antibodies made by  
20 recombinant means such as chimeric antibodies, wherein the variable region and constant region are derived from different species, and CDR-grafted antibodies, wherein the complementarity determining region is derived from a different species, as described in US Patents 4,816,567 and 5,225,539. Chimeric antibodies may be prepared by splicing genes for a mouse antibody molecule having a desired antigen specificity together with genes for a human antibody molecule having the  
25 desired biological activity, such as activation of human complement and mediation of ADCC (Morrison *et al. Proc. Natl. Acad. Sci. USA* 81:6851, 1984; Neuberger *et al. Nature* 312:604, 1984; Takeda *et al. Nature* 314:452, 1985).

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard  
30 techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*,

Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to

Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

5           It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or  
10   linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

          A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent  
15   No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating  
20   compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

          A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of  
25   a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

#### T CELLS

30           Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral

blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated  
5 humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific  
10 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a  
15 variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell  
20 proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of  
25 the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Prostate-specific protein-specific T cells may be expanded using  
30 standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.



For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide  
5 corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

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#### PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds  
15 and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally  
20 described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the  
25 composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression  
30 systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression

in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA

or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- $\gamma$ , TNF $\alpha$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10 ) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example,

*Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take-up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface  
5 receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone  
10 marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into  
15 dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this  
20 nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II  
25 MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place  
30 *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection

that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the prostate-specific polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

#### CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer

cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate  
5 antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in*  
10 *vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte,  
15 fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies  
20 have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back  
25 into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established  
30 using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered

over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50%  
5 above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-  
10 vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active  
15 compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be  
20 evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or  
25 more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the  
30 agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer.

In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, 5 *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized 10 on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, 15 protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full 20 length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or 25 disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" 30 refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a



membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of  
5 binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the  
10 binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may  
15 be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The  
20 amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween  
25 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer.  
30 Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by

assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains  
5 a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of  
10 time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group  
15 (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a  
20 signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is  
25 determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest  
30 to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along

the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that

expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may  
5 be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate-specific polypeptide (*e.g.*, 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater  
10 and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to  
15 amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization  
20 assay to detect the presence of polynucleotide encoding the protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in  
25 length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15  
30 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Techniques for both PCR based assays and hybridization assays

are well known in the art (*see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989*).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue,  
5 and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or  
10 greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or  
15 polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such  
20 assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate-specific protein markers  
25 may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or  
30 alternatively, assays for proteins provided herein may be combined with assays for other known tumor antigens.

## DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For  
5 example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or  
10 indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or  
15 hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

## EXAMPLES

### EXAMPLE 1

#### 5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate  
10 tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA was then purified using a Qiagen oligotex spin column mRNA  
15 purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into  
20 ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained  $1.64 \times 10^7$   
25 independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained  $3.3 \times 10^6$  independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

30 cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as

follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H<sub>2</sub>O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As  
5 recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with  
10 BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H<sub>2</sub>O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and  
15 incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H<sub>2</sub>O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA  
20 was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and  
25 grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively,  
30 with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.



The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1  $\mu$ g each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA

library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show  
5 some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid  
10 sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided  
15 in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating  
20 sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in  
25 SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated  
30

clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 5 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further 10 analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the 15 identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 20 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA<sup>+</sup> RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4288, 1D-25 4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

30 cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni,

Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively.

## EXAMPLE 2

### DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2  $\mu$ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using  $\beta$ -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the  $\beta$ -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for each

reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney,

but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

### EXAMPLE 3

#### ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of



2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The putative full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 525.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483.

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led

to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

#### EXAMPLE 4

##### SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

#### EXAMPLE 5

##### FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the

SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

5

Table I  
Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-idoitol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most

recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350, 351 and 353-365.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

## EXAMPLE 6

## PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

5           6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

          Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID  
10 NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100 $\mu$ g of P2S#12 and 120 $\mu$ g of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6 x 10<sup>6</sup> cells/ml in complete media (RPMI-1640; Gibco  
15 BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10<sup>-5</sup> M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml  $\beta$ 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 $\mu$ g/ml dextran sulfate and 25 $\mu$ g/ml LPS for 3 days). Six days later, cells (5 x  
20 10<sup>5</sup>/ml) were restimulated with 2.5 x 10<sup>6</sup>/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and 3 x 10<sup>6</sup>/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

          P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb  
25 tumor cells (1 x 10<sup>4</sup> cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( 5 x 10<sup>5</sup> cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in  
30 Figure 1.

          This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.



6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells ( $5 \times 10^5$ /ml) were restimulated with  $2.5 \times 10^6$ /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown  
5 in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

#### EXAMPLE 7

##### 10 PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100  $\mu$ g P501S in the vector VR1012 either intramuscularly or intradermally.  
15 The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at  
20 least one naturally processed HLA-A2-restricted CTL epitope.

#### EXAMPLE 8

##### 25 ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8<sup>+</sup> T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van  
30 Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8<sup>+</sup> T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a  $\gamma$ -interferon

ELISPOT assay (*see* Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on  $10^4$  fibroblasts in the presence of 3  $\mu\text{g/ml}$  human  $\beta_2$ -microglobulin and 1  $\mu\text{g/ml}$  P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml  $\gamma$ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a  $\gamma$ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

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## EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES  
IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8<sup>+</sup> cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts retrovirally transduced

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to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays ( $^{51}\text{Cr}$  release) and interferon-gamma production (Interferon-gamma Elispot; *see* above and Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

#### EXAMPLE 10

##### IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE-SPECIFIC ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100  $\mu\text{g}$  of p5 peptide together with 140  $\mu\text{g}$  of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived

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## GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH PROSTATE-SPECIFIC ANTIGEN

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- $\gamma$  ELISPOT analysis as described above. Using a panel of  
5 HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a  
10 multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3  $\mu$ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that  
15 specifically produced interferon- $\gamma$  when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- $\gamma$  in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

20 To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN- $\gamma$  ELISPOT assays against these A2Kb targets transduced with the "library" of P501S  
25 fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were  
30 also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN- $\gamma$  assay. Only peptides

P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

5 In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40  
10 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as  
15 demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-  
20 P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

### EXAMPLE 13

#### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

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This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in  
30 prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97%



of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

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## EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS  
BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which

expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II

Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups:

10 Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group

15 libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (*see* Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III  
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV  
Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP

440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

## EXAMPLE 15

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY  
ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

## EXAMPLE 16

## FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane

filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four  
5 sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene.

## EXAMPLE 17

### PROTEIN EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

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This example describes the expression and purification of the prostate-specific antigen P501S in *E. coli*, baculovirus and mammalian cells.

#### a) Expression in *E. coli*

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Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an  
20 antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min,  
25 and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was  
30 induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A

(Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

5           An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR  
10 product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

          The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands  
15 were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

          A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen  
20 Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

25           The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD\_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c) Expression of P501S in mammalian cells

Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture



was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 µl of GenePorter was diluted in 500 µl of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 µg of plasmid DNA that was diluted in 500 µl of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

#### EXAMPLE 18

#### PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

##### 20 a) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to

generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant ( $\mu\text{g/ml}$ )
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1  $\mu\text{g/ml}$ , followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate

specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr.

HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson Immunoresearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

#### **b) Preparation and Characterization of Antibodies against P503S**

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits

and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

5

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows.

The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further

15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the

appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

#### 5 **c) Preparation and Characterization of Antibodies against P703P**

Rabbits were immunized with either a truncated (P703Ptrl; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptrl attached to a solid support. Rabbit monoclonal  
10 antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal  
20 antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

25 The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk<sup>-/-</sup> cells either untransfected or transfected with a plasmid

expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

#### EXAMPLE 19

##### CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains. Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as



described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparagine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e. intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM

sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above.

To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al. Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

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From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

30

## CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536;

(b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

(c) complements of any of the sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID No: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

4. An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein  
5 comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413,  
10 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate-specific protein, or a  
15 variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396,  
20 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one  
25 of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530,  
30 531, 533, 535 and 536.

7. An isolated polynucleotide comprising a sequence that hybridizes under moderately stringent conditions to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector comprising a polynucleotide according to any one of claims 4-8.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein, the protein comprising an amino acid sequence encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536 or a complement of any of the foregoing polynucleotide sequences.

12. A monoclonal antibody that specifically binds to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 519, 520, 522 and 539-551.
- 5 13. A monoclonal antibody comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.
- 10 14. A fusion protein comprising at least one polypeptide according to claim 1.
- 15 15. A fusion protein according to claim 14, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.
- 16 16. A fusion protein according to claim 14, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.
- 17 17. A fusion protein according to claim 14, wherein the fusion protein comprises an affinity tag.
- 20 18. An isolated polynucleotide encoding a fusion protein according to claim 14.
- 25 19.. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:
- (a) a polypeptide according to claim 1;
  - (b) a polynucleotide according to claim 4;
  - (c) an antibody according to any one of claims 11-13;
  - 30 (d) a fusion protein according to claim 14; and

(e) a polynucleotide according to claim 18.

20. A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

- 5 (a) a polypeptide according to claim 1;  
(b) a polynucleotide according to claim 4;  
(c) an antibody according to any one of claims 11-13;  
(d) a fusion protein according to claim 14; and  
(e) a polynucleotide according to claim 18.

10

21. A vaccine according to claim 20, wherein the immunostimulant is an adjuvant.

22. A vaccine according to claim 20, wherein the immunostimulant  
15 induces a predominantly Type I response.

23. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 19.

20

24. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

25. A pharmaceutical composition comprising an antigen-presenting cell  
25 that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

26. A pharmaceutical composition according to claim 25, wherein the antigen presenting cell is a dendritic cell or a macrophage.



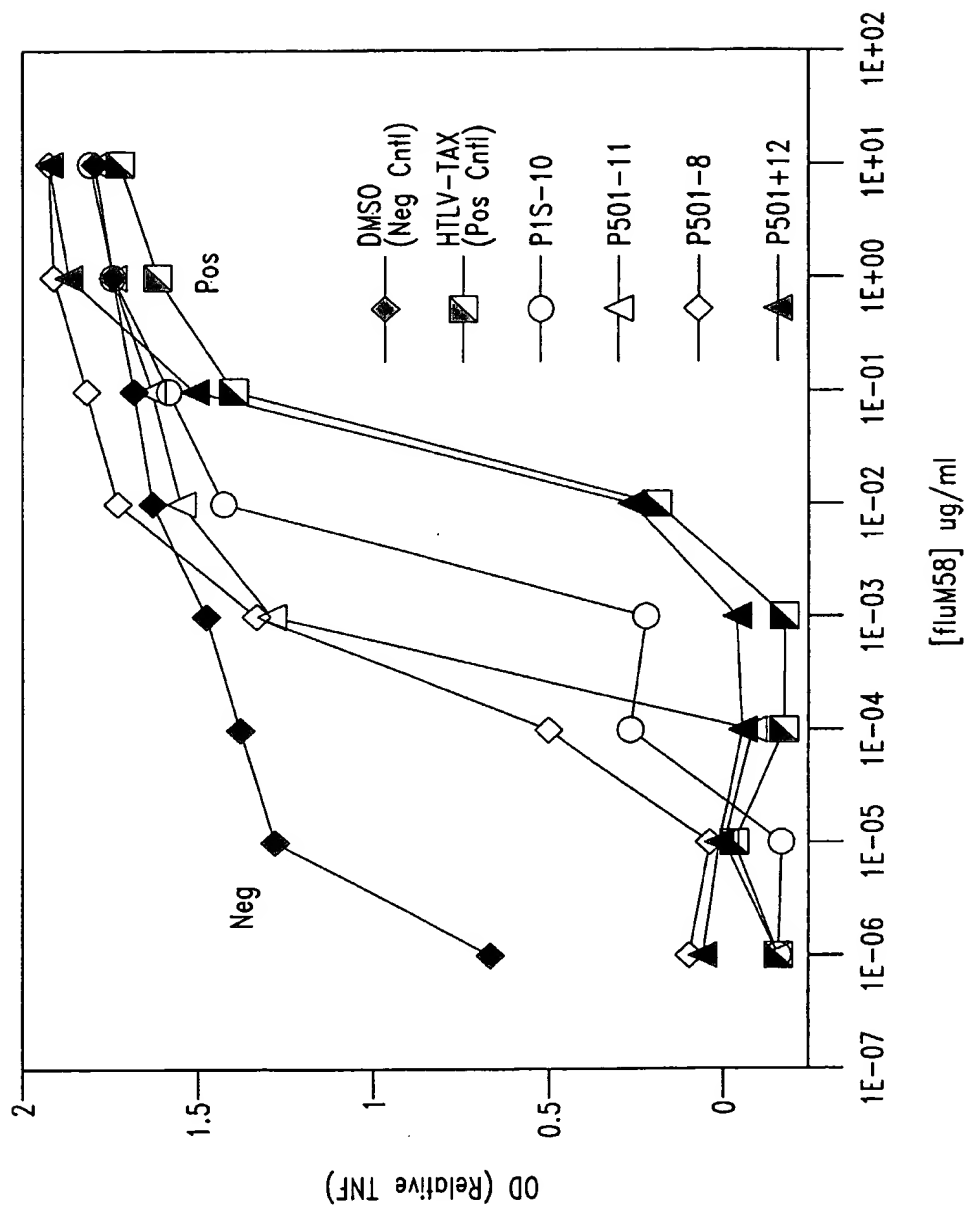


Fig. 3

27. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.

5 28. A vaccine according to claim 27, wherein the immunostimulant is an adjuvant.

29. A vaccine according to claim 27, wherein the immunostimulant induces a predominantly Type I response.

10

30. A vaccine according to claim 27, wherein the antigen-presenting cell is a dendritic cell.

31. A method for inhibiting the development of a cancer in a patient,  
15 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, and thereby inhibiting the development of a cancer in the patient.

20

32. A method according to claim 31, wherein the antigen-presenting cell is a dendritic cell.

33. A method according to any one of claims 23, 24 and 31, wherein the  
25 cancer is prostate cancer.

34. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the protein comprises an amino acid sequence that is  
30 encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

5                    wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate-specific protein from the sample.

35.     A method according to claim 34, wherein the biological sample is  
10    blood or a fraction thereof.

36.     A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

15

37.     A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (i)     a polypeptide according to claim 1;
- 20        (ii)    a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;
- (iii)    a polynucleotide encoding a polypeptide of (i) or (ii); and
- (iv)    an antigen presenting cell that expresses a polypeptide of (i) or (ii),
- 25           under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

38.     An isolated T cell population, comprising T cells prepared according to the method of claim 37.

30

39. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 38.

5 40. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;  
10 (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); or  
15 (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

20

41. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

25 (i) a polypeptide according to claim 1;  
(ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

30 (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

(b) cloning at least one proliferated cell to provide cloned T cells; and

5 (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

42. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

10 (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NO: 1-111,  
15 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii) complements of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent; and

20 (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

43. A method according to claim 42, wherein the binding agent is an antibody.

25

44. A method according to claim 43, wherein the antibody is a monoclonal antibody.

45. A method according to claim 42, wherein the cancer is prostate  
30 cancer.

46. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

- 5 (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;
- 10 (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the  
15 amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

47. A method according to claim 46, wherein the binding agent is an antibody.

20

48. A method according to claim 47, wherein the antibody is a monoclonal antibody.

49. A method according to claim 46, wherein the cancer is a prostate  
25 cancer.

50. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- 30 (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein,

wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

5 (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

10

51. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15 52. A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

53. A method for monitoring the progression of a cancer in a patient,  
20 comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315,  
25 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from  
30 the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

5                    54. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

10                   55. A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

15                   56. A diagnostic kit, comprising:  
                     (a) one or more antibodies according to claim 11; and  
                     (b) a detection reagent comprising a reporter group.

                     57. A kit according to claim 56, wherein the antibodies are immobilized on a solid support.

20                   58. A kit according to claim 56, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

25                   59. A kit according to claim 56, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

30                   60. An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45,



47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 5 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides.

61. A oligonucleotide according to claim 60, wherein the oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO: 10 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536.

15

62. A diagnostic kit, comprising:

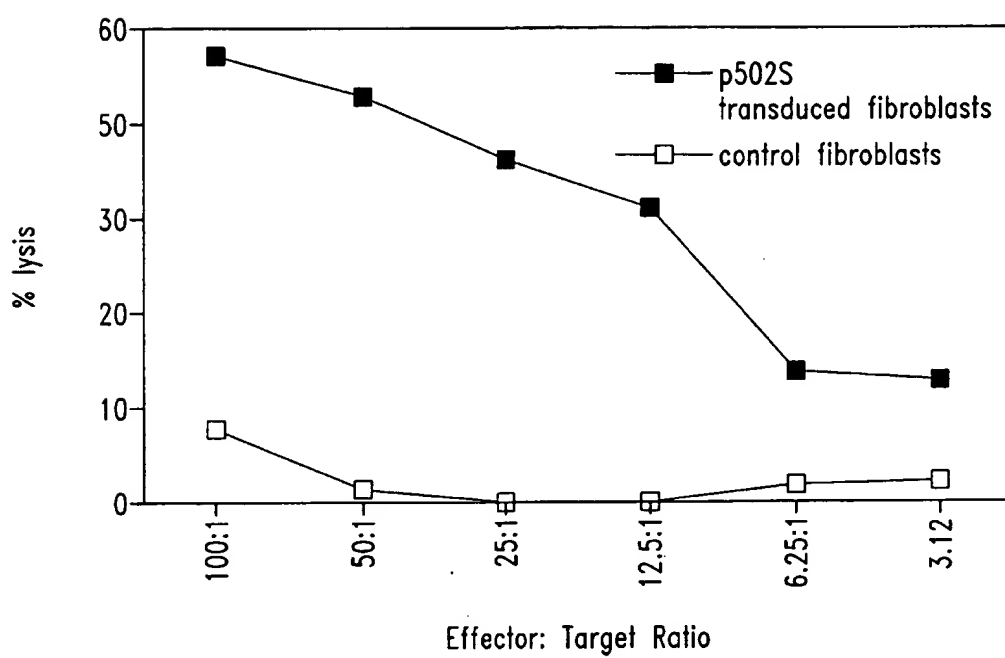
(a) an oligonucleotide according to claim 61; and

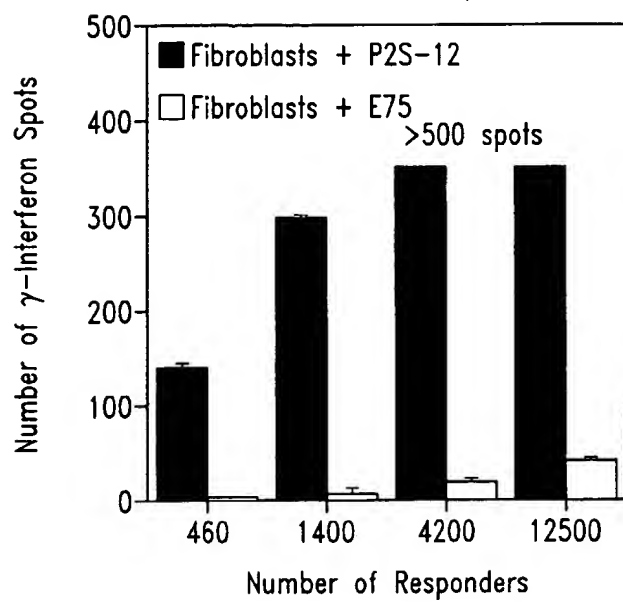
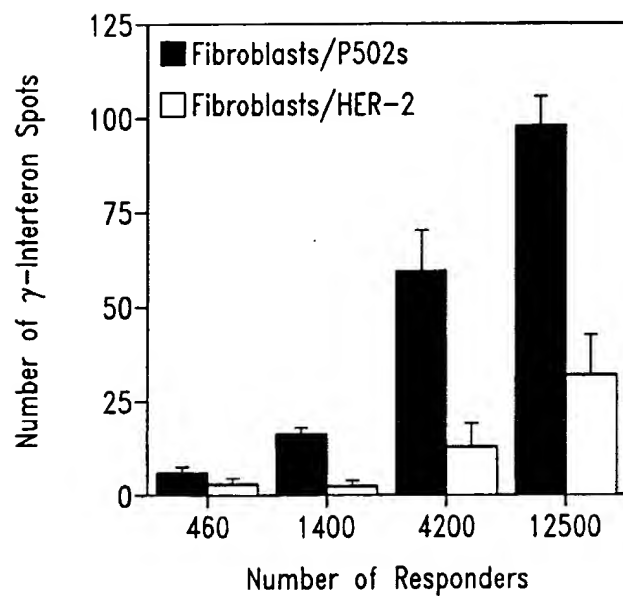
(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

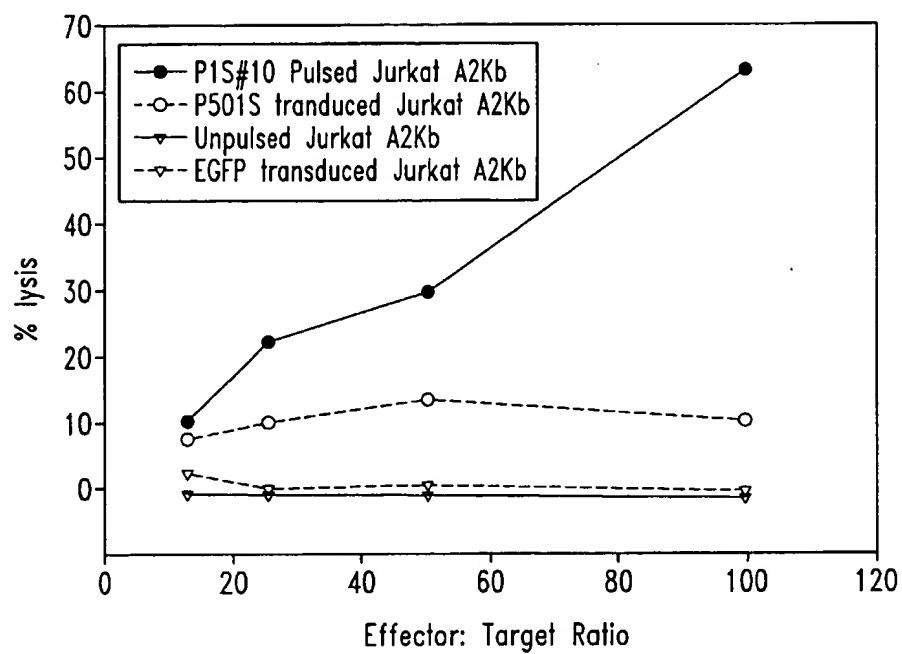
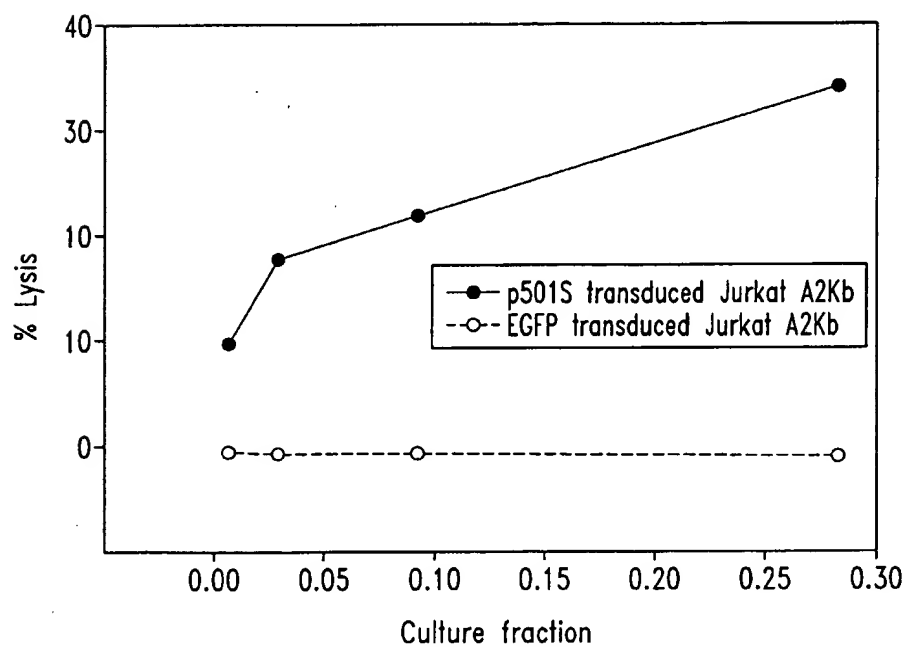
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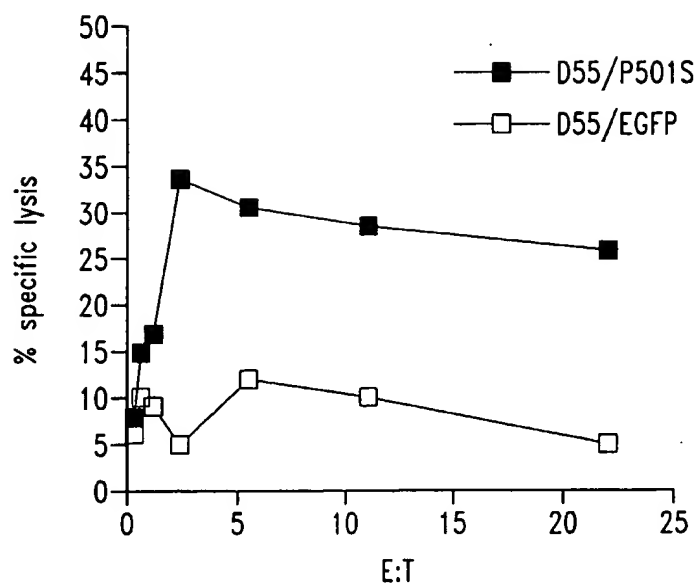
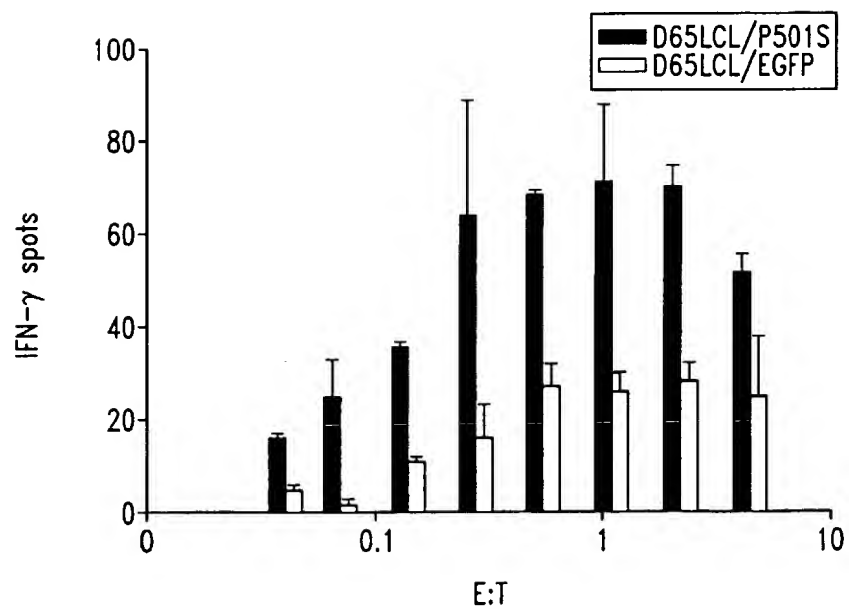
63. A host cell according to claim 10, wherein the cell is selected from the group consisting of: *E. coli*, baculovirus and mammalian cells.

64. A recombinant protein produced by a host cell according to claim 25 10.

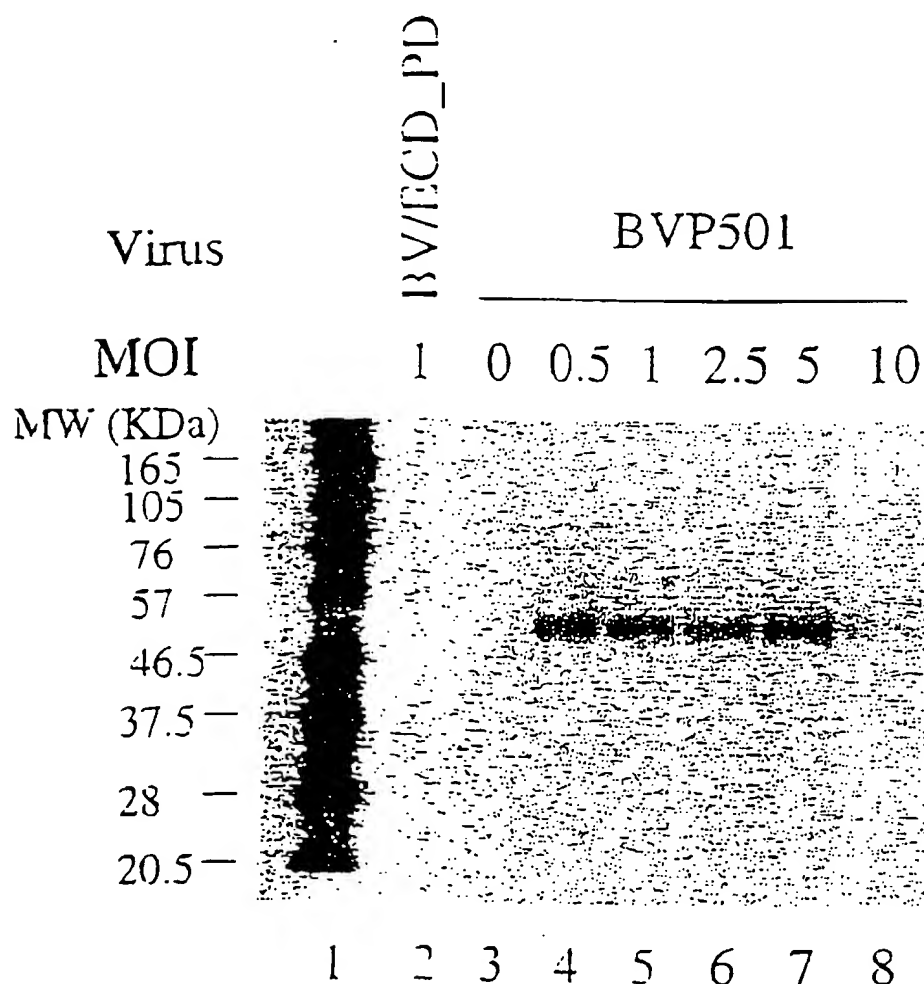
*Fig. 1*

*Fig. 2A**Fig. 2B*

*Fig. 4**Fig. 5*

*Fig. 6A**Fig. 6B*

# Expression of P501S by the Baculovirus Expression System



0.6 million high 5 cells in 8-well plate were infected with an unrelated control virus BV/ECD\_PD (lane 2), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4 - 8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

Fig. 7

**Figure 8. Mapping of the epitope recognized by 10E3-G4-D3**

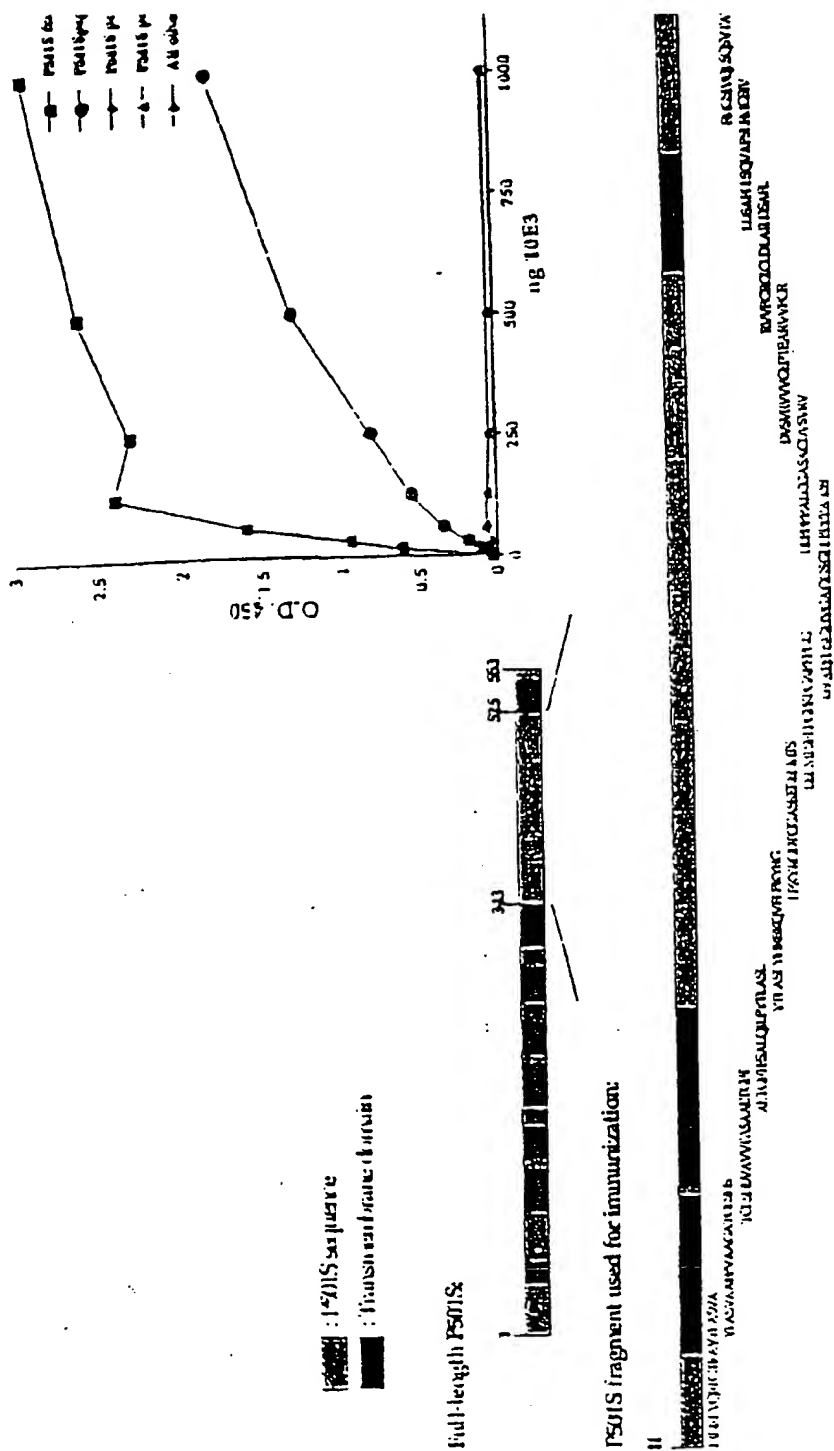


Fig. 8

Schematic of P501S with predicted  
transmembrane, cytoplasmic, and extracellular regions

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HQLCCRMPTLR LFVAELCSWMALMTFTLFYTD VGEGLYQGVPRAPGTEARRHYDEGVR  
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VTAYMVSAAGLGLVAIYFAT QVVF DKSDLAKYSA

Underlined sequence: Predicted transmembrane domain; **Bold sequence:**  
 Predicted extracellular domain; *Italic sequence:* Predicted intracellular  
 domain. Sequence in bold/underlined: used generate polyclonal rabbit  
 serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and I. Simon  
 (1998) Principles Governing Amino Acid Composition of Integral Membrane  
 Proteins: Applications to topology Prediction. J. Mol Biol. 283, 489-506.

*Fig. 9*



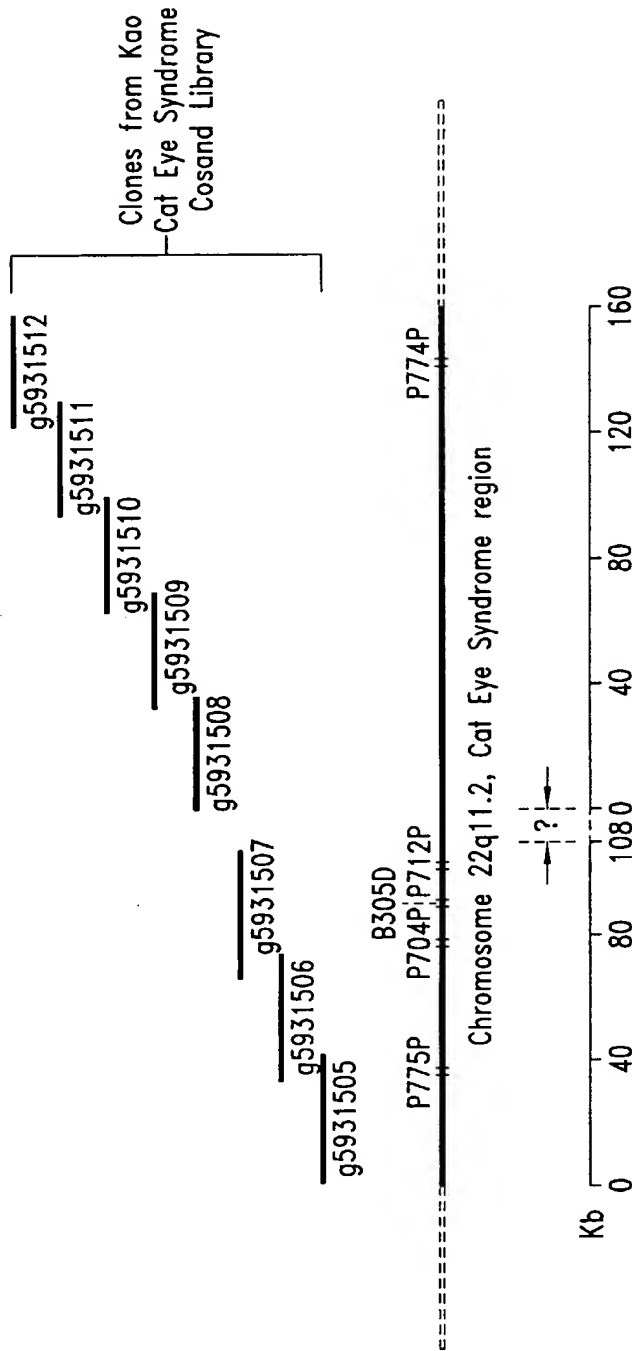


Fig. 10

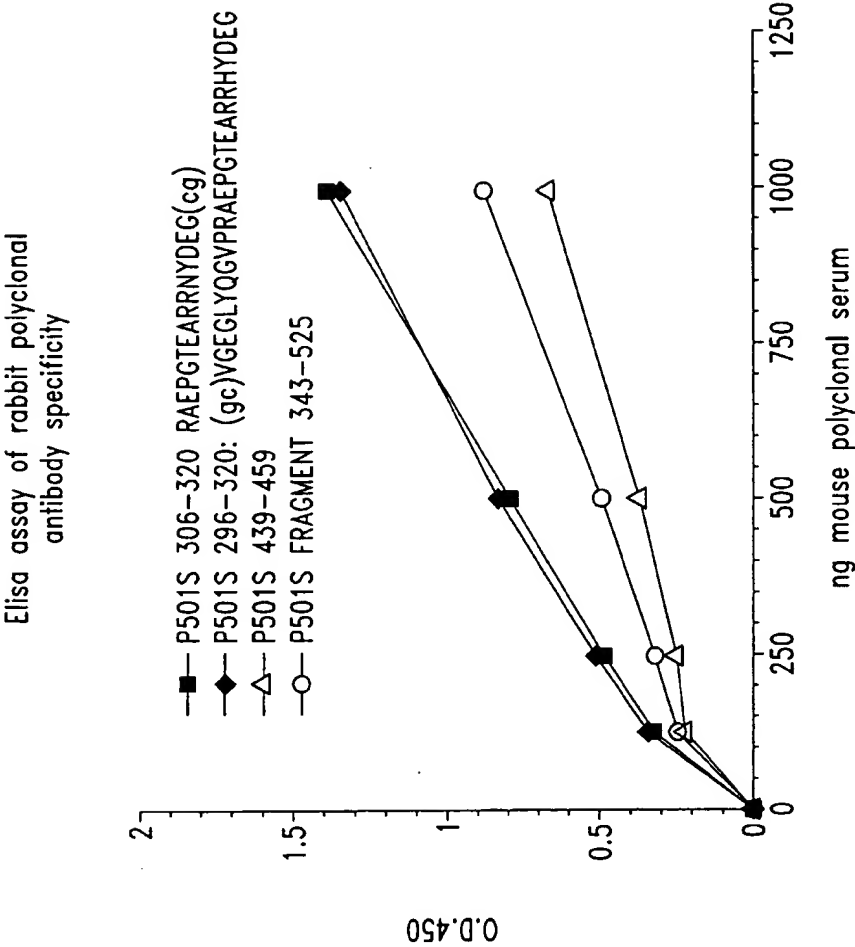


Fig. 11

## SEQUENCE LISTING

<110> Corixa Corporation  
 Xu, Jiangchun  
 Dillon, Davin C.  
 Mitcham, Jennifer L.  
 Harlocker, Susan Louise  
 Jiang Yuqui  
 Reed, Steven G.  
 Kalos, Michael  
 Fanger, Gary  
 Retter, Mark  
 Solk, John  
 Day, Craig  
 Skeiky, Yasir A.W.  
 Wang, Aijun

<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND  
 DIAGNOSIS OF PROSTATE CANCER

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tgtaaagtga	aatattagtt	ggcggatgaa	gcagatagtg	aggaaagttg	agccaataat	180
gacgtgaagt	ccgtggaagc	ctgtggctac	aaaaaatggt	gagccgtaga	tgccgtcgga	240
aatggtgaag	ggagactcga	agtactctga	ggcttgtagg	agggtaaaat	agagaccag	300

taaaattgta	ataagcagt	cttgaattat	ttggtttcgg	ttgttttcta	ttagactatg	360
gtgagctcag	gtgattgata	ctcctgatgc	gagtaatacg	gatgtgttta	ggagtgggac	420
ttctagggga	tttagcgggg	tgatgcctgt	tgggggccag	tgccctccta	ggtggggggt	480
aggggctagg	ctggagtggg	aaaaggetca	gaaaaatcct	gcgaagaaaa	aaacttctga	540
ggtaataaat	aggattatcc	cgtatcgaag	gccttttttg	acagggtggg	tgtgggtggc	600
ttgggtatgt	ctttctcgtg	ttacatcgcg	ccatcattgg	tatatggtta	gtgtgttggg	660
ttantangg	ctantatgaa	gaacttttgg	antggaatta	aatcaatngc	ttggccggaa	720
gtcattanga	nggetnaaaa	ggccctgtta	ngggtctggg	ctnggtttta	cccnacccat	780
ggaatncnc	ccccggacna	ntgnatccct	attctttaa			818

&lt;210&gt; 7

&lt;211&gt; 817

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (817)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 7

tttttttttt	tttttttttt	tggtctctaga	gggggtagag	gggggtgctat	agggtaaata	60
cgggccctat	ttcaaagatt	tttaggggaa	ttaattctag	gacgatgggt	atgaaactgt	120
ggtttgcctc	acagatttca	gagcattgac	cgtagtatac	ccccggtcgt	gtagcgggtga	180
aagtggtttg	gttttagacgt	ccgggaattg	catctgtttt	taagcctaata	gtggggacag	240
ctcatgagtg	caagacgtct	tgtgatgtaa	ttattatacn	aatgggggct	tcaatcggga	300
gtactactcg	attgtcaacg	tcaaggagtc	gcaggtcgcc	tggttctagg	aataatgggg	360
gaagtatgta	ggaattgaag	attaatccgc	cgtagtcggg	gttctcctag	gttcaatacc	420
attgggtggc	aattgatttg	atggtaaggg	gagggatcgt	tgaactcgtc	tgttatgtaa	480
aggatncctt	ngggatggga	aggcnatnaa	ggactangga	tnaatggcgg	gcangatatt	540
tcaaacngtc	tctanttcct	gaaacgtctg	aaatgttaata	aanaattaan	tttngttatt	600
gaetnttnng	gaaaagggtc	tacaggacta	gaaaccaaata	angaaaanta	atnntaangg	660
cnttatcctn	aaaggtnata	accnctccta	tnatcccacc	caatngnatt	ccccacnncn	720
acnattggat	ncceccanttc	canaaaanggc	cnccccccgg	tgnannccnc	cttttgttcc	780
cttnantgan	ggttattcnc	ccctngcntt	atcance			817

&lt;210&gt; 8

&lt;211&gt; 799

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (799)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 8

catttccggg	tttactttct	aaggaaagcc	gagcgggaagc	tgctaacgtg	ggaatcggtg	60
cataaggaga	actttctgct	ggcagcgct	agggacaagc	gggagagcga	ctccgagcgt	120
ctgaagcgca	cgtcccagaa	ggtggacttg	gcaactgaaac	agctgggaca	catccgcgag	180
tacgaacagc	gcctgaaagt	gctggagcgg	gaggtccagc	agtgtagccg	cgtcctgggg	240
tgggtggccg	angcctgan	cgtctgcct	tgctgcccc	angtgggccc	ccaccccttg	300
acctgctgg	gtccaaacac	tgagccctgc	tggcggactt	caagganaac	ccccacangg	360
ggattttgct	cctanantaa	ggctcatctg	ggcctcgccc	ccccacctg	gttggccttg	420
tctttgagnt	gagcccatg	tccatctggg	ccactgtcng	gaccaccttt	ngggagtgtt	480
ctccttacaa	ccacannatg	cccggtccct	cccggaaccc	antccancc	tgngaaggat	540
caagnccctn	atccactnnt	nctanaaccg	gccnccnccg	cngtggaaac	cnccttntgt	600
tcttttctnt	tnagggttaa	tnnccgcttg	gccttnccan	ngtcctnccn	nttttccnnt	660

gttnaaattg	ttangcnccc	nccnntcccn	cnnncnnan	cccgaccenn	annttnnann	720
ncctgggggt	ncnncngat	tgaccenncc	ncctntant	tgcnttnggg	nncntgccc	780
ctttccctct	nggganncg					799

<210> 9  
 <211> 801  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(801)  
 <223> n = A,T,C or G

<400> 9						
acgccttgat	cctcccaggc	tgggactggt	tctgggagga	gccgggcatg	ctgtggtttg	60
taangatgac	actcccaaag	gtggtcctga	cagtggccca	gatggacatg	gggctcacct	120
caaggacaag	gccaccagg	gcgggggccc	aagccacat	gacccctact	ctatgagcaa	180
aatccctgt	gggggcttct	ccttgaagtc	cgccancagg	gctcagtctt	tggaccang	240
caggtcatgg	ggttgtngnc	caactggggg	ccncaacgca	aaanggcnc	gggcctcngn	300
cacccatccc	angacgcggc	tacactnctg	gacctccnc	tccaccactt	tcatgcgctg	360
ttcntaccgg	cgnatntgtc	ccanctgttt	cngtgccnac	tccancttct	nggacgtgcg	420
ctacatacgc	ccggantcnc	netcccgtt	tgtccctatc	cacgtncan	caacaaattt	480
cnccntantg	caccnattcc	cacntttnc	agntttcnc	nncngcttc	ctntaaaaag	540
ggttganccc	cggaaaatnc	cccaaagggg	gggggcccng	tacccaactn	ccccctnata	600
gctgaantcc	ccatnaccnn	gnctcnatgg	anccntccnt	tttaannacn	ttctnaactt	660
gggaanance	ctcgnccntn	ccccnttaa	tccnccttg	cnangnnnt	ccccnntcc	720
ncccnntng	gcntntnann	cnaaaaaggc	ccnnnancaa	tctcctnncn	cctcanttcg	780
ccanccctcg	aaatcgccn	c				801

<210> 10  
 <211> 789  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(789)  
 <223> n = A,T,C or G

<400> 10						
cagtctatnt	ggccagtgtg	gcagctttcc	ctgtggctgc	cggtgccaca	tgccctgtccc	60
acagtgtggc	cggtggtgaca	gcttcagccg	ccctcaccgg	gttcaccttc	tcagccctgc	120
agatcctgcc	ctacacactg	gcctccctct	accaccggga	gaagcagggtg	ttcctgccca	180
aataccgagg	ggacactgga	ggtgctagca	gtgaggacag	cctgatgacc	agcttcctgc	240
caggccctaa	gcctggagct	cccttcoccta	atggacacgt	gggtgctgga	ggcagtggcc	300
tgtcccacc	tccaccgcg	ctctgcgggg	cctctgcctg	tgatgtctcc	gtacgtgtgg	360
tggtgggtga	gcccaccgan	gccaggggtg	ttccgggccc	gggcatctgc	ctggacctcg	420
ccatcctgga	tagtgcttcc	tgtgtgccca	ngtgggccca	tccctgttta	tgggctccat	480
tgtccagctc	agccagtctg	tcactgccta	tatggtgtct	gccgcaggcc	tgggtctggt	540
cccatttact	ttgctacaca	ggtantattt	gacaagaacg	anttggccaa	atactcagcg	600
ttaaaaaatt	ccagcaacat	tgggggtgga	aggcctgcct	cactgggtcc	aactccccgc	660
tccgtttaac	cccatggggc	tgccggcttg	gccgccaatt	tctgttgctg	ccaaantnat	720
gtggctctct	gctgccacct	gttgctggct	gaagtgcnta	cngcncanct	nggggggtng	780
gnggttccc						789

<210> 11  
 <211> 772

<212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(772)  
 <223> n = A,T,C or G

<400> 11

cccaccctac	ccaaatatta	gacaccaaca	cagaaaagct	agcaatggat	tcccttctac	60
tttggttaaat	aaataagtta	aatatattaaa	tgcctgtgtc	tctgtgatgg	caacagaagg	120
accaacaggc	cacatcctga	taaaaggtaa	gaggggggtg	gatcagcaaa	aagacagtgc	180
tgtgggctga	ggggacctgg	ttcttgtgtg	ttgccccctca	ggactcttcc	cctacaaata	240
actttcatat	gttcaaatcc	catggaggag	tgtttcatcc	tagaaactcc	catgcaagag	300
ctacattaaa	cgaagctgca	ggttaagggg	cttanagatg	ggaaaccagg	tgactgagtt	360
tattcagctc	ccaaaaaacc	ttctctaggt	gtgtctcaac	taggaggcta	gctgttaacc	420
ctgagcctgg	gtaatccacc	tcagagtgcc	ccgcattcca	gtgcatggaa	cccttctggc	480
ctccctgtat	aagtcacagac	tgaaccctcc	ttggaaggnc	tccagtcagg	cagccctana	540
aactggggaa	aaaagaaaag	gacgccccan	ccccagctg	tgcantctacg	cacctcaaca	600
gcacaggggtg	gcagcaaaaa	aaccacttta	ctttggcaca	aacaaaaaact	nggggggggca	660
accccgccac	cccnangggg	gttaacagga	ancngggnaa	cntggaaccc	aattnaggca	720
ggcccncac	ccnaatntt	gctgggaaat	ttttcctccc	ctaaattntt	tc	772

<210> 12  
 <211> 751  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

<400> 12

gccccaatte	cagctgccac	accacccacg	gtgactgcat	tagttcggat	gtcatataaaa	60
agctgattga	agcaaccctc	tacttttttg	tcgtgagcct	tttgcttggg	gcagggtttca	120
ttggctgtgt	tggtgacgtt	gtcattgcaa	cagaatgggg	gaaaggcact	gttctctttg	180
aagtanggtg	agtcctcaaa	atccgtatag	ttggtgaagc	cacagcactt	gagccctttc	240
atgggtgggt	tccacacttg	agtgaagtct	tcctgggaac	cataatcttt	cttgatggca	300
ggcactacca	gcaacgtcag	ggaagtgtct	agccattgtg	gtgtacacca	aggcgaccac	360
agcagctgcn	acctcagcaa	tgaagatgan	gaggangatg	aagaagaacg	tcncgagggc	420
acacttgctc	tcagtcttan	caccatanca	gccntgaaa	accaananca	aagaccacna	480
cnccggctgc	gatgaagaaa	tnaccccnccg	ttgacaaaact	tgcatggcac	tggganccac	540
agtggcccn	aaaatcttca	aaaaggatgc	cccactnatt	gaccccccaa	atgccactg	600
ccaacagggg	ctgccccacn	cncnnaacga	tgancnatt	gnacaagatc	tncntggctc	660
tnatnaacnt	gaacctgcn	tngtggctcc	tgttcaggnc	cnnggcctga	cttctnaann	720
aangaactcn	gaagncccca	cngganann	g			751

<210> 13  
 <211> 729  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(729)  
 <223> n = A,T,C or G



```

<400> 13
gagccaggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgcctt      60
tgtggancct cagcagtncc ctctttcaga actcantgcc aaganccctg aacaggagcc      120
accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt      180
ctgtgtgggt cagccctggt ggcagtgggc atctgggtgt caatcgatgg ggcacacctt      240
ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc      300
ctcatcgcat ccggcggtgt ggtcttagct ctaggtttcc tgggctgcta tgggtctaag      360
actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct      420
gaggttgcaa tgcgtgggtc gccttgggtg acaccacaat ggctgagcac ttcttgacgt      480
tgctggtaat gccctgccatc aanaaaagat tatgggttcc caggaaactc tcaactcaagt      540
gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt      600
gaagantcac ctacttcaaa gaaaaanagt cctttccccc atttctgttg caattgacaa      660
acgtcccaaa cacagccaat tgaaaacctg caccacaacc aaanggttcc ccaaccanaa      720
attnaaggg                                     729

```

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<210> 14
<211> 816
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (816)
<223> n = A,T,C or G

```

```

<400> 14
tgctcttctt caaagttggt cttgttgcca taacaaccac cataggtaaa gcgggagcag      60
tgttcgctga aggggttgta gtaccagcgc gggatgctct ccttgagagc tcctgtgtct      120
ggcaggtcca cgcagtgcc tttgtcactg gggaaatgga tgcgctggag ctctgcaaa      180
ccactcgtgt atttttcaca ggcagcctcg tccgacgcgt cggggcagtt ggggggtgtct      240
tcacactcca ggaaactgtc natgcagcag ccattgctgc agcggaaactg ggtgggctga      300
cangtgccag agcacactgg atggcgctt tccatgnnan gggccctgng ggaaagtccc      360
tganccccaan anctgcctct caaangcccc acctgcaca ccccgacagg ctagaatgga      420
atcttcttcc cgaaaggtag ttnttcttgt tgcccaancc anccccntaa acaaactctt      480
gcanatctgc tccngggggg tcntantacc ancgtgggaa aagaacccca ggcngcgaac      540
caancttgtt tggatnecaa gcnataatct nctnttctgc ttggtggaca gcaccantna      600
ctgtnnanct ttagncnttg gtccctnttg gttgnncttg aacctaaten cennccaact      660
gggacaaggt aantngcctt ccttttaatt cccnancntn ccccttggtt tgggggtttt      720
cncnctccta cccagaaaan nccgtgttcc cccccaacta ggggcnanaa cennntnttc      780
cacaaccctn cccacccac ggggtcngnt ggttng                                     816

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```

<210> 15
<211> 783
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1) ... (783)
<223> n = A,T,C or G

```

```

<400> 15
ccaaggcctg ggcaggcata nacttgaagg tacaaccacca ggaaccctg gtgctgaagg      60
atgtggaaaa cacagattgg cgcctactgc ggggtgacac ggatgtcagg gtagagagga      120
aagacccaaa ccagggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga      180
cagtgactag ctacagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca      240
ccaagcagac agaagactac tgcctcgcat ccaacaangt gggtcgctgc cggggctctt      300
tcccacgtg gtactatgac cccacggagc agatctgcaa gagtttcgtt tatggagggt      360

```

```

gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcnggggtg 420
tgcaagggtg gcctttgana ngcanctctg gggctcangc gactttcccc cagggcccct 480
ccatggaaaag gcgcatcca ntgttctctg gcacctgtca gccacccag ttcgctgca 540
ncaatggctg ctgcatcnac antttcctng aattgtgaca acacccccca ntgccccaa 600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccg 660
cncctcctnt tccccnntn aacaaagggc nctngcctt gaactgccc aaccnnggaa 720
tctnccnngg aaaaantncc ccccttggtt cctnnaance cctccncaaa anctncccc 780
ccc 783

```

```

<210> 16
<211> 801
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

```

```

<400> 16
gccccaatc cagctgccac accaccacag gtgactgcat tagttcggat gtcatacaaa 60
agctgattga agcaaccctc tacttttttg tctgagcct tttgcttgg gcaggtttca 120
ttggctgtgt tggtagcgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg 180
aagttagggg agtccctcaa atccgtatag ttggtgaagc cacagcactt gagccctttc 240
atgggtgggt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca 300
ggcactacca gcaacgtcag gaagtgtcga gccattgtgg tgtacaccaa ggcgaccaca 360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca 420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg 480
ccngctgcga atgaaagaaa ntaccacagt tgacaaactg catggccact ggacgacagt 540
tggcccgaan atcttcagaa aagggatgcc ccctcgattg aacaccana tgcccactgc 600
cnacaggggt gcnccnccn gaaagaatga gccattgaag aagatcctc ntggctttaa 660
tgaactgaaa ccntgcatgg tggccctgtt tcagggtctt tggcagtga ttctganaaa 720
aaggaacngc ntnagcccc ccaaangana aaacaccccc ggggtgttgc ctgaattggc 780
ggccaaggan cctgccccn g 801

```

```

<210> 17
<211> 740
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(740)
<223> n = A,T,C or G

```

```

<400> 17
gtgagagcca ggcgtccctc tgctgcccc ctgagtggca acacccggga gctgttttgt 60
cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg 120
agccaccatg cagtgttca gcttcattaa gaccatgatg atcctcttca atttgctcat 180
ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc 240
ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta 300
cttctcatc gcagccggcg ttgtgggtct tgctcttggg ttccctgggt gctatgggtc 360
taagacggag agcaagtgtg cctcgtgac gttcttcttc atcctctcc tcatcttcat 420
tgctgaagtt gcagctgctg tggctgcctt ggtgtacacc acaatggctg aaccattcct 480
gacgttgctg gtantgctg ccatcaanaa agattatggg ttcccaggaa aaattcactc 540
aantntggaa caccnccatg aaaagggctc caatttctgn tggcttcccc aactataccg 600
gaattttgaa agantcnccc tacttccaaa aaaaaanant tgcctttnc cccnttctgt 660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaaa 720

```

caaaaaaant nnaaggggtn

740

<210> 18  
 <211> 802  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(802)  
 <223> n = A,T,C or G

<400> 18  
 ccgctgggttg cgctgggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca 60  
 caaggtcttc cagctgccgc acattacgca gggcaagagc ctccagcaac actgcatatg 120  
 ggatacactt tacttttagca gccagggtga caactgagag gtgtcgaagc ttattcttct 180  
 gagcctctgt tagtggagga agattccggg cttcagctaa gtagtcagcg tatgtcccat 240  
 aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa 300  
 cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat 360  
 ggatgagtgt ggccagcgtt gccccttgg ccgacttggc taggagcaga aattgctcct 420  
 ggttctgccc tgtcaccttc acttcgcac tcatcactgc actgagtgtg ggggacttgg 480  
 gctcaggatg tccagagacg tggttccgcc cctcncctta atgacaccgn ccanncaacc 540  
 gtcggctccc gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cncacttgc 600  
 aanccttcgtc nggcccattg aattcacccn accggaactn gtangatcca ctntttctat 660  
 aaccggncgc caccgcnnnt ggaactccac tctntttncc ttacttgag ggttaaggtc 720  
 acccttnncc ttaccttggg ccaaaccntn centgtgtcg anatngtnaa tcnggncna 780  
 tnccanccnc atangaagcc ng 802

<210> 19  
 <211> 731  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(731)  
 <223> n = A,T,C or G

<400> 19  
 cnaagcttcc aggtnacggg ccgcnaance tgaccnagg tancanaang cagnncgcgg 60  
 gagcccaccg tcacgnngng gngtctttat nggagggggc ggagccacat cnetggacnt 120  
 cntgacccca actcccncnc ncnantgca gtgatgagtg cagaactgaa ggtnacgtgg 180  
 caggaaccaa gancaaannc tgcctcnntc caagtcggcn naggggggcg ggctggccac 240  
 gncatecnt cnagtgtcgn aaagccccnn cctgtctact tgtttgaga acngcnnnga 300  
 catgcccagn gttanataac nggcngagag tnantttgcc tctcccttcc ggctgcgcan 360  
 cgngtntgct tagnggacat aacctgacta cttaactgaa ccnngaate tncnccct 420  
 ccaactaagt cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta 480  
 aagtgtaccc catncccaat gtntgctnga ngctctgncc tgcnttangt tcggtcctgg 540  
 gaagacctat caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc 600  
 cnncnntcca agggggggnc ggcccccaat ccccccaacc ntnaattnan tttancccn 660  
 ccccnggcc cggcctttta cnancntcnn nnacnnggna aaaccnnngc tttncccaac 720  
 nnaatccncc t 731

<210> 20  
 <211> 754  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (754)  
 <223> n = A,T,C or G

<400> 20  
 .tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60  
 caacccccctc ntccaaatnn ccntttccgg gnggggggttc caaacccaan ttanntttgg 120  
 annttaaatt aaatnttntt tggnggnnna ancnaatgt nangaaagt naaccanta 180  
 tnancctnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctcgg 240  
 aaatngttna nggaaaaccc aanttctent aagggtgttt gaaggntnaa tnaaaanccc 300  
 nnccaattgt ttttngccac gcctgaatta attggnntcc gntgttttcc nttaaaanaa 360  
 ggnnancccc ggttantnaa tcccccnnc cccaattata ccganttttt ttngaattgg 420  
 gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc ccccntcggg 480  
 ggttngggnc aggnncnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc 540  
 ccaggntgag nntnggggtt ncccccccc cangggccct ctcgnanagt tgggggttgg 600  
 ggggcctggg attttntttc cctntttnc tcccccccc ccnggganag aggttngngt 660  
 tttgntcnc ggccccnccn aaganttttn ccganttnan ttaaaccnt gcctnggcga 720  
 agtccttgn agggntaaan ggccccctnn cggg 754

<210> 21  
 <211> 755  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (755)  
 <223> n = A,T,C or G

<400> 21  
 atcancccat gaccccnac nngggacnc tcancggnc nnncnaccnc eggcnatca 60  
 nngtnagnnc actncnnttn natcaacccc cncnactac gcccnananc cnacgcnta 120  
 nncanatncc actganngcg cgangtngan ngagaaact nataccanag ncaccanacn 180  
 ccagctgtcc nanaangect nnnatacngg nnnatccaat ntgnancctc cnaagtattn 240  
 nncnnanacat gatthtctn anccgattac ccntncccc tanccctcc cccccaacna 300  
 cgaaggcnct ggnccnaagg nngcgnccc ccgctagnt ccenncaagt cncnnccta 360  
 aactcanccn nattacnccg ttentgagta tctctcccg aatctcacc tactcaactc 420  
 aaaaanacn gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480  
 ttagnggtcc ntnaanctc ctaatacttc cagctnccct tcnccaattt ccnaanggt 540  
 ctttcngaca gcatnttttg gttcccnntt gggttcttan ngaattgccc ttctntgaac 600  
 gggtcctct tttccttcgg ttancctggn ttcnccggc cagttattat ttcccnnttt 660  
 aaattcctnc cntttanttt tggccttcna aacccccggc cttgaaaacg gccccctggg 720  
 aaaagggtgt tttganaaaa tttttgtttt gttcc 755

<210> 22  
 <211> 849  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (849)  
 <223> n = A,T,C or G

<400> 22  
 tttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt 60  
 acgctnggan taangcgacc cgantttctag ganncnccct aaaatcanac tgtgaagatn 120

atcctgnnna	cggaanggtc	accggnggat	nntgctaggg	tgncnctcc	cannncttn	180
cataactcng	nggccctgcc	caccaccttc	ggcgcccng	ngnccgggcc	cgggtcattn	240
gnnttaaccn	cactnngcna	ncggtttccn	ncccnncng	accnngcgga	tccggggtn	300
tctgtcttcc	cctgnagncn	anaaantggg	ccnccgnccc	ctttaccctt	nnacaagcca	360
cngcctctta	nccnngccc	ccctccant	nngggggact	gcnannget	cgttntctng	420
nnaccccnnn	gggtncctcg	gttgtcgant	cnaccgnang	ccanggattc	cnaaggaagg	480
tgcgttnttg	gccccctacc	ttcgctnccg	nncacccttc	ccgacnanga	nccgctcccc	540
cnncnccngg	cctcncctcg	caacacccgc	ncctcncgt	ncggnnnccc	ccccacccgc	600
nccctcncnc	ngnccgnanc	ctcncncnc	gtctcannca	ccaccccgcc	ccgccaggcc	660
ntcanccacn	ggnggacnng	nagcncntc	gcncgcgcg	gcgnccctt	cgccncngaa	720
ctncntcngg	ccantnncgc	tcaancnna	cnaaacgccg	ctgcgcggcc	cgnagcgncc	780
ncctcncga	gtcctcccg	cttcnacc	angnttccn	cgaggacacn	nnaccccgcc	840
nncangcgg						849

<210> 23  
 <211> 872  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (872)  
 <223> n = A,T,C or G

<400> 23						
gcgcaaaacta	tacttcgctc	gnactcgtgc	gcctcgetnc	tcttttcttc	cgcaaccatg	60
tctgacnanc	ccgattnggc	ngatatcnan	aagntcganc	agtccaaact	gantaacaca	120
cacacnncan	aganaaatcc	nctgccttcc	anagtanacn	attgaacnng	agaaccangc	180
nggcgaatcg	taatnaggcg	tgcgcgcgca	atntgtcncc	gtttattntn	ccagctcnc	240
ctnccnacc	tacntcttcn	nagctgtcnn	acccctngtn	cgnaccccc	naggtcggga	300
tggggttttn	nntgaccng	cnnccctcc	cccttccat	nacganccnc	ccgcaccacc	360
nanngcncgc	ncccggnct	cttcgcnc	ctgtcctntn	ccctgtngc	ctggcncngn	420
accgcattga	ccctcgcnn	ctnccngaaa	ncgnanacgt	ccgggttggn	annacgctg	480
tgggnnngcg	tctgcncgc	gttccttcn	ncncttcca	ccatcttnt	tacngggct	540
ccnccgctc	tccnncacnc	cctgggacgc	tntcctntgc	cccccttnac	tccccccctt	600
cgncgtgncc	cgnccccacc	ntcatttnca	nacgntcttc	acaannccct	ggntnntctc	660
cnanccngcn	gtcancnag	ggaagggngg	ggnnccnntg	nttgacgttg	ngngangtc	720
cgaanantcc	tccnctcan	cncctaccct	cgggcggnct	ctcngttnc	aacttancaa	780
ntctcccccg	ngngcncntc	tcagcctcnc	ccncccnct	ctctgcantg	tntctgtctc	840
tnaccmntac	gantnttcgn	cncctcttt	cc			872

<210> 24  
 <211> 815  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (815)  
 <223> n = A,T,C or G

<400> 24						
gcattgcaagc	ttgagtattc	tatagngtca	cctaaatanc	ttggcntaat	catggtcnta	60
nctgncttcc	tgtgtcaaat	gtatacnaa	tanatatgaa	tctnatntga	caaganngta	120
tctnccatta	gtaacaantg	tnntgtccat	cctgtcngan	canattccca	tnnatnccgn	180
cgcattcncn	gncantatn	taatngggaa	ntcnntnnn	ncacnncat	ctatcctncc	240
gncctctgac	tggngagat	ggatnantt	tnntntgacc	nacatgttca	tcttggattn	300
aanaccccc	cgcnccac	cggttngng	cnagcnnct	ccaagacctc	ctgtggagg	360

aacctgcgtc	aganncatca	aacntgggaa	acccgcnncc	angtnnaagt	ngnnncanan	420
gateccgtcc	aggnttnacc	atccccttcnc	agcgcceccct	ttngtgcctt	anagnnagc	480
gtgtccnanc	cnctcaacat	ganacgcgcc	agnccanccg	caattnggca	caatgtcgnc	540
gaaccccccta	gggggantna	tncaaanccc	caggattgtc	cncncangaa	atcccnanc	600
cccncctac	ccncttttg	gacngtgacc	aantcccga	gtncagtc	ggccngnctc	660
ccccaccggt	nncntgggg	gggtgaanct	cngnntcanc	cngncgaggn	ntcgnaagga	720
accggncctn	ggncgaann	ancnntcnga	agngcncnt	cgtataaccc	cccctcncca	780
nccnacngnt	agntcccccc	cngggtnccg	aangg			815

&lt;210&gt; 25

&lt;211&gt; 775

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(775)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 25

ccgagatgtc	tcgtccgtg	gccttagctg	tgctcgcgt	actctctctt	tctggcctgg	60
aggctatcca	gcgtactcca	aagattcagg	tttactcacg	tcattccagca	gagaatggaa	120
agtcaaattt	cctgaattgc	tatgtgtctg	ggtttcatcc	atccgacatt	gaanttgact	180
tactgaagaa	tgganagaga	attgaaaaag	tggagcattc	agacttgtct	ttcagcaagg	240
actggtcttt	ctatctcntg	tactacactg	aattcacccc	caactgaaaa	gatgagtatg	300
cctgcccgtg	gaaccatgtg	actttgtcac	agcccaagat	agttaagtgg	gatcgagaca	360
tgtaagcagn	cnnatggaa	gtttgaagat	gccgcatttg	gattggatga	attccaaatt	420
ctgcttgctt	gcntttta	antgatatgc	ntatacaccc	taccctttat	gnccccaaat	480
tgtaggggtt	acatnantgt	tcnctnngga	catgatcttc	ctttataant	ccnccnttcg	540
aattgcccgt	cncccngttn	ngaagtgttc	cnaaaccacg	gttggtctcc	ccaggtcncc	600
tcttacggaa	gggcctgggc	cnctttncaa	gggtggggga	accnaaaatt	tcncttntgc	660
cccccnccca	cnctcttng	nncncanttt	ggaacccttc	cnattccctt	tggeectcna	720
nccttnncta	anaaaacttn	aaancgtngc	naaanntttn	acttcccccc	ttacc	775

&lt;210&gt; 26

&lt;211&gt; 820

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(820)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 26

anattantac	agtgtaatct	tttcccagag	gtgtgtanag	ggaacggggc	ctagaggcat	60
cccanagata	ncttatanca	acagtgtctt	gaccaagagc	tgctgggcac	atttcctgca	120
gaaaagggtg	cggtcccat	cactcctcct	ctcccatagc	catcccagag	gggtgagtag	180
ccatcangcc	ttcgggtggga	gggagtcang	gaaacaacan	accacagagc	anacagacca	240
ntgatgacca	tgggcgggag	cgagcctctt	ccctgnaccg	gggtggcana	nganagccta	300
nctgaggggt	cacactataa	acgttaacga	ccnagatnan	cacctgtctc	aagtgcaccc	360
ttcctacctg	acnaccagn	accnnaact	gncgcctggg	gacagcnctg	ggancagcta	420
acnnagcact	cacctgcccc	cccatggccg	tnccgntccc	tggtcctgnc	aagggaagct	480
ccctgttgga	attncgggga	naccaaggga	nccccctcct	ccanctgtga	aggaaaaann	540
gatggaattt	tncccttcctg	gcnntcccc	tcttcttcta	cacgccccct	nntactcntc	600
tccctctntt	ntcctgnenc	acttttnacc	ccnnnatctc	ccttnattga	tcggannctn	660
ganattccac	tnncgcctnc	cntcnatcng	naanaacnaa	nactntctna	cccnggggat	720
gggnncctcg	ntcatcctct	ctttttcnct	accnccnntt	ctttgcctct	ccttnyatca	780

tccaacntc gntggcentn cccccccnnn tcctttcccc

820

<210> 27  
 <211> 818  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(818)  
 <223> n = A,T,C or G

<400> 27  
 tctgggtgat ggcctcttcc tcctcagggc cctctgactg ctctgggcca aagaatctct 60  
 tgtttcttct ccgagcccca ggcagcgggtg attcagccct gcccaacctg attctgatga 120  
 ctgctgatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggaggggcgc 180  
 ctgctgagca ctcccgcccc tcacctgcc cagccctgc catgagctct gggctgggtc 240  
 tccgcctcca gggttctgct ctccangca ngccancaa tggtcgtggg ccacactggc 300  
 ttcttctctc cccntccctg gctctganc tctgtcttcc tgtcctgtgc angcnccttg 360  
 gatctcagtt tccctcctc anngaactct gttctgann tcttcantta actntgantt 420  
 tatnaccnan tggnetgtnc tgcnnactt taatgggcn gaccggctaa tccctccctc 480  
 nctcccttcc anttcnnnna accngcttnc cntctctcc centancccg ccngggaanc 540  
 ctcccttgcc ctnaccangg gccnnnaccg ccctnnctn ggggggcnnng gtnnctncnc 600  
 ctgntnnccc cncctcncnt tncctcgtec cncnncgcg nngcannttc ncngtcccn 660  
 tnnctcttcn ngntctcgnaa ngntcncntn tnnnnngncn ngntnntncn tccctctcnc 720  
 cnnntgnang tnnttnnnnc ncngnncccc nnnnnnnnn nggnntnnn tctncncngc 780  
 cccnncccc ngnattaagg cctccnntct ccggccnc 818

<210> 28  
 <211> 731  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(731)  
 <223> n = A,T,C or G

<400> 28  
 aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg 60  
 tccaacatg anggtgnngt tctcttttga angaggggtg ngtttttann ccnggtgggt 120  
 gattnaaccc cattgtatgg agnnaaagg ttttagggat ttttcggctc ttatcagtat 180  
 ntanattcct gtnaatcgga aaatnatntt tcnnenggaa aatnttgctc ccatccgnaa 240  
 attnctcccg ggtagtgcatt nttngggggn cngccangtt tcccaggctg ctanaatcgt 300  
 actaaagntt naagtgggan tncaaatgaa aacctnnac agagnatccn taccgactg 360  
 tnnnttncct tcgcccctntg actctgcnn agcccaatac ccnngnngnat gtcncccnng 420  
 nnngcgnenc tgaaannnnc tcgnggctnn gancatcang gggtttcgca tcaaaagcnn 480  
 cgtttcncat naaggcactt tngcctcctc caaccnctng ccctcnncca tttngccgtc 540  
 nggttcncct acgctnntng cncctnnntn ganattttnc ccgcctnggg naancctcct 600  
 gnaatgggta gggnccttntc ttttnaccnn gnggtntact aatcnnctnc acgctnctt 660  
 tctnaccccc cccctttttt caatcccanc ggcnaatggg gtctccccnn cgangggggg 720  
 nnnccannc c 731

<210> 29  
 <211> 822  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(822)  
 <223> n = A,T,C or G

<400> 29  
 actagtccag tgtgggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat 60  
 cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt 120  
 atntntacnc tcatannect cnnnacccac tccctcttaa ccctactgt gcctatngcn 180  
 tnnctantct ntgcgcctn cnanccaccn gtggggccnac cncnngnatt ctcnatctcc 240  
 tcnccatntn gcctananta ngtncatacc ctataacctac nccaatgcta nnnctaancn 300  
 tccatnantt annntaacta ccactgaant ngactttcnc atnanctcct aatttgaatc 360  
 tactctgact cccacngcct annnattagc ancttcccc nacnatntct caaccaaadc 420  
 ntcaacaacc tatctantct ttcnccaacc nttncctcog atcccccnac aacccccctc 480  
 ccaaataccc nccacctgac nctaaccen caccatcccc gcaagccnan ggnccatttan 540  
 ccactggaat cacnatngga naaaaaaaac ccnaactctc tancncnnat ctccttaana 600  
 aatnctcctn naatttactn ncantnccat caancccaac tgaaacnnaa cccctgtttt 660  
 tanatccctt ctttcgaaaa ccnacccttt annncccaac ctttngggcc cccccnctnc 720  
 ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaaggcna anannntccg 780  
 canatcctat cccttanttn ggggnccctt nccnggggcc cc 822

<210> 30  
 <211> 787  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(787)  
 <223> n = A,T,C or G

<400> 30  
 cggccgcctg ctctggcaca tgctctctga atggcatcaa aagtgatgga ctgcccattg 60  
 ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt 120  
 gtctgcagga tttgatgtct gaagtctgtg agtgtggctt ggagctcctc atctacatna 180  
 gctggaagcc ctggagggcc tctctcgcca gctccccct tctctccacg ctctccangg 240  
 acaccagggg ctccaggcag cccattattc ccagnangac atgggtgttc tccacgcgga 300  
 cccatggggc ctgnaaggcc aggggtctct ttgacaccat ctctcccgte ctgctggca 360  
 ggccgtggga tccactantt ctanaacggg cgccaccnng gtgggagctc cagcttttgt 420  
 tccnttaat gaaggttaat tgencgcttg gcgtaatcat nggtcanaac tntttcctgt 480  
 gtgaaattgt ttntcccctc ncnattccnc ncnacatacn aaccgggaan cataaagtgt 540  
 taaagcctgg gggtngcctn nngaataaac tnaactcaat taattgctgt ggctcatggc 600  
 ccgctttccn ttcnngaaaa ctgtentccc ctgcnttntt gaatcggcca cccccnggg 660  
 aaaagcgggt tgcnttttng ggggntcctt ccncttcccc cctcnctaan cctnccgct 720  
 cggctgttnc nggtngcggg gaangggnat nnnctccnnc naagggggng agnnngntat 780  
 ccccaaa 787

<210> 31  
 <211> 799  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(799)  
 <223> n = A,T,C or G

<400> 31



tttttttttt	tttttttggc	gatgctactg	tttaattgca	ggaggtgggg	gtgtgtgtac	60
catgtaccag	ggctattaga	agcaagaagg	aaggaggag	ggcagagcgc	cctgctgagc	120
aacaaaggac	tcctgcagcc	ttctctgtct	gtctcttggc	gcaggcacat	ggggaggcct	180
cccgagggt	gggggccacc	agtccagggt	tgggagcact	acanggggtg	ggagtgggtg	240
gtggctggtn	cnaatggcct	gncacanatc	cctacgattc	ttgacacctg	gatttcacca	300
ggggaccttc	tgttctccca	nggnaacttc	ntnnatctcn	aaagaacaca	actgtttctt	360
cngcanttct	ggctgttcat	ggaaagcaca	ggtgtccnat	ttnggctggg	acttggtaca	420
tatggttccg	gcccacctct	ccntcnaaa	aagtaattca	ccccccccc	ccntctnttg	480
cctgggacct	taantaccca	caccggaact	canttantta	ttcatcttng	gntgggcttg	540
ntnatcnccn	cctgaangcg	ccaagtgtgaa	aggccacgcc	gtncnccnctc	cccatagnan	600
ntttttnent	canctaagtc	cccccnnggc	aacnatccaa	tccccccccc	tggggggcccc	660
agcccanggc	ccccgncctg	ggnnnccngn	cncgnantcc	ccaggntctc	ccantcngnc	720
ccnnngcncc	cccgacgca	gaacanaagg	ntngagccnc	cgcannnnnn	nggtnncnac	780
ctcgcccccc	ccnncgng					799

&lt;210&gt; 32

&lt;211&gt; 789

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(789)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 32

tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	60
tttttncnag	ggcagggttta	ttgacaacct	cncgggacac	aancaggctg	gggacaggac	120
ggcaacaggc	tccggcgggc	gcggcggcgg	ccctacctgc	ggtaccaa	ntgcagcctc	180
cgctcccgc	tgatnttcc	ctgcagctgc	aggatgcct	aaaacagggc	ctcgccntn	240
ggtgggcacc	ctgggatttn	aatttccacg	ggcacaatgc	ggtcgcancc	cctcaccacc	300
nattaggaat	agtgtgtntta	ccnccnccg	ttggencact	cccnttgga	accacttntc	360
gcggctccgg	catctggtct	taaaccttgc	aaacnctggg	gccctctttt	tggttantnt	420
nccngccaca	atcatnactc	agactggcnc	gggctggccc	caaaaaancn	ccccaaaacc	480
ggncatgtc	ttnnccgggt	tgctgcnatn	tncatcacct	cccgggcnca	ncaggncaac	540
caaaaagttc	ttngggcccn	caaaaaanc	ccggggggnc	ccagtttcaa	caaagtcac	600
ccccttggcc	cccaaactct	cccccgntt	netgggtttg	ggaaccacg	cctctnnctt	660
tggnnggcaa	gntggntccc	ccttcgggce	cccggtgggc	ccnctctaa	ngaaaaacnc	720
ntcctnnnca	ccatcccccc	nngnnacgnc	tancaangna	tccctttttt	tanaaacggg	780
ccccccnccg						789

&lt;210&gt; 33

&lt;211&gt; 793

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(793)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 33

gacagaacat	gttgatgggt	ggagcacctt	tctatacgac	ttacaggaca	gcagatgggg	60
aattcatggc	tggtggagca	atanaacccc	agttctacga	gctgtgatc	aaaggacttg	120
gactaaagtc	tgatgaactt	cccaatcaga	tgagcatgga	tgattggcca	gaaatgaana	180
agaagtttgc	agatgtat	gcaaagaaga	cgaaggcaga	gtggtgtcaa	atctttgacg	240
gcacagatgc	ctgtgtgact	ccggttctga	cttttgagga	ggttgttcat	catgatcaca	300
acaangaacg	gggctcgttt	atcaccantg	aggagcagga	cgtgagcccc	cgcctgtcac	360

ctctgctggt	aaacacccca	gccatccctt	ctttcaaaa	ggatccacta	cttctagagc	420
ggncgccacc	gcggtggagc	tccagctttt	gttcccttta	gtgagggtta	attgcgcgct	480
tggcgtaatc	atggtcatan	ctgtttcctg	tgtgaaattg	ttatccgctc	acaattccac	540
acaacatacg	anccggaagc	atnaaatTTT	aaagcctggg	ggtngcctaa	tgantgaact	600
nactcacatt	aattggcttt	gcgctcactg	cccgttttcc	agtcgcgaaa	acctgtcctt	660
gccagctgcc	nttaatgaat	cnggccaccc	cccggggaaa	aggcngtttg	cttnttgggg	720
cgcncctccc	gctttctcgc	ttcctgaant	ccttcccccc	ggtctttcgg	cttgcggcna	780
acggtatcna	cct					793

&lt;210&gt; 34

&lt;211&gt; 756

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(756)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 34

gccgcgaccg	gcatgtacga	gcaactcaag	ggcgagtggg	accgtaaaa	ccccaatctt	60
ancaagtgcg	gggaanagct	gggtcgactc	aagctagttc	ttctggagct	caacttcttg	120
ccaaccacag	ggaccaagct	gaccaaacag	cagctaattc	tggcccgtga	catactggag	180
atcggggccc	aatggagcat	cctacgcaan	gacatccctc	ccttcgagcg	ctacatggcc	240
cagctcaaat	gctactactt	tgattacaan	gagcagctcc	ccgagtcagc	ctatatgcac	300
cagctcttgg	gcctcaacct	cctcttcctg	ctgtcccaga	accgggtggc	tgantnccac	360
acgganttgg	ancggtgcg	tgcccaanga	catacanacc	aatgtctaca	tcnaccacca	420
gtgtcctgga	gcaatactga	tgganggcag	ctaccncaaa	gtnttcctgg	ccnagggtaa	480
catccccgcg	cgagagctac	accttcttca	ttgacatcct	gctcgacact	atcaggggatg	540
aaaatcgcn	ggttgctcca	gaaaggctnc	aanaanatcc	ttttcnctga	aggcccccg	600
atnncnctag	ncatgaatcg	gcccgccatc	gcggtgganc	ctccaacctt	tcgttnccct	660
ttactgaggg	ttnattgccg	cccttgccgt	tatcatgggtc	acnccngttn	cctgtgttga	720
aattnttaac	ccccacaaat	tccacgcena	cattnng			756

&lt;210&gt; 35

&lt;211&gt; 834

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(834)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 35

ggggatctct	anatenacct	gnatgcattg	ttgtcggtgt	ggtcgctgtc	gatgaanatg	60
aacaggatct	tgcccttgaa	gctctcggtc	gctgtnttta	agttgctcag	tctgccgtca	120
tagtcagaca	cnctcttggg	caaaaaacan	caggatntga	gtcttgattt	cacctccaat	180
aatcttcnng	gctgtctgct	cggtgaactc	gatgaacnang	ggcagctggg	tgtgtntgat	240
aaantccanc	angttctcct	tggtgacctc	cccttcaaa	ttgttccggc	cttcatcaaa	300
cttctnnaan	angannancc	canctttgtc	gagctggnat	ttgganaaca	cgtcactggt	360
ggaaactgat	cccaaatggg	atgtcatcca	tcgctctgc	tgcttgcaaa	aaacttgctt	420
ggcncaaatc	cgactcccn	tccttgaaa	aagccnatca	cacccccctc	cctggactcc	480
nncaangact	ctnecgctnc	cccntccnng	cagggttggt	ggcannccgg	gcccntgcgc	540
ttcttcagcc	agttcacnat	nttcatcagc	ccctctgcc	gctgtntat	tccttggggg	600
ggaanccgtc	tctcccttcc	tgaannaact	ttgaccgtng	gaatagccgc	gcntcnccnt	660
acntnctggg	ccgggttcaa	antccctccn	ttgncnntcn	cctcggggcca	ttctggattt	720
nccnaacttt	ttccttcccc	cncnccnccg	ngtttggnnt	tttcatnggg	ccccaactct	780

gctnttggcc antcccctgg gggcntntan cccccctnt ggtcccntng ggcc 834

<210> 36  
<211> 814  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)... (814)  
<223> n = A,T,C or G

<400> 36  
cggnccgttt ccngccgcgc cccgtttcca tgacnaaggc tcccttcang ttaaatacnn 60  
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgceca 120  
naacgccaac tcaggccatt cctaccaaag gaagaaaggc tgggtctctcc accccctgta 180  
ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact 240  
aatggaaaaa aaaaataaac aanagggttt gttctcatgg ctgcccaccg cagcctggca 300  
ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgctctt ttggacatca 360  
ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc 420  
antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc 480  
aggggangtc ntttncagtg gatctgccaa anantaccen tatcatcnnt gaataaaaaag 540  
gccccgaac ganatgcttc cancanctt taagacccat aatcctngaa ccatggtgcc 600  
cttcgggtct gatccnaaag gaatgttctt gggctccant cctcctttg ttncttacgt 660  
tgtnttgac cntgtctngn atnacccaan tganatcccc ngaagcacc tncctctggc 720  
atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcncnnaan 780  
ggngaactca agaaggtctn ngaaaaacca cncn 814

<210> 37  
<211> 760  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)... (760)  
<223> n = A,T,C or G

<400> 37  
gcatgctgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg 60  
gcgcagtgtt cgctgaagg gttgtagtac cagcgcgga tgctctcctt gcagagtcct 120  
gtgtctggca ggtccacgca atgccctttg tccctgggga aatggatgcg ctggagctcg 180  
tcnaanccac tcgtgtatctt ttacangca gcctcctccg aagctccgg gcagttgggg 240  
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt 300  
gggctgacag gtgccagaac acactggatn ggcttttcca tggaaaggcc tgggggaaat 360  
cncctnancc caaactgcct ctcaaaggcc accttgca caacgacagg ctagaaatgc 420  
actcttcttc ccaaaggtag ttgttcttgg tgcccaagca ncctccanca aaccaaaanc 480  
ttgcaaaatc tgctccgtgg gggcatnnn taccanggtt ggggaaanaa acccgcnngn 540  
gancncctt gtttgaatgc naaggnaata atcctcctgt cttgcttggg tggaaanagca 600  
caattgaact gttaacnttg ggcgngttc cncnnggtg gtctgaaact aatcacgctc 660  
actggaaaaa ggtangtgcc ttccttgaat tcccaaannt cccctngntt tgggtntttt 720  
ctcctctncc ctaaaaatcg tnttcccccc cntanggcg 760

<210> 38  
<211> 724  
<212> DNA  
<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(724)  
 <223> n = A,T,C or G

<400> 38  
 tttttttttt tttttttttt tttttttttt ttttttaaaa cccctccat tgaatgaaaa 60  
 cttccnaaat tgtccaaccc cctcnnccaa atnnccattt cggggggggg gtcccaaac 120  
 caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa 180  
 aatttaaccc attatnaact taaatnccn gaaaccntg gnttccaaaa atttttaacc 240  
 cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaagggt 300  
 ngatttaaac ccccttnant tnttttnacc cnngnctnaa ntatttngnt tccgggtgtt 360  
 tcctnttaan cntnggtaac tcccgntaat gaannnccct aanccaatta aaccgaattt 420  
 tttttgaatt ggaaattccn ngggaattna cgggggtttt tcccntttgg gggccatncc 480  
 cccnctttcg ggggtttggg ntaggttgaa ttttttnang nccccaaaaa ncccccaana 540  
 aaaaaactcc caagnnttaa ttngaantnc ccccttccca ggccttttgg gaaaggnggg 600  
 tttntggggg ccngggantt cnttccccn ttncncccc cccccnggt aaanggttat 660  
 ngnttttggg ttttgggccc cttnanggac ctccggatn gaaattaaat ccccggnngc 720  
 gccg 724

<210> 39  
 <211> 751  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

<400> 39  
 tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgctgca 60  
 caacacaata tttatttcat ttgtttcttt tatttcattt tatttgttg ctgctgctgt 120  
 tttatttatt tttactgaaa gtgagaggga acttttgtgg ccttttttcc tttttctgta 180  
 ggccgcctta agcttttctaa atttggaaca tctaagcaag ctgaanggaa aaggggggtt 240  
 cgcaaaatca ctcgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300  
 ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc ttttaattana 360  
 cttgggggtt ccttccccc accaaccnccn ctgacaaaaa gtgccngccc tcaaatnatg 420  
 tccgggcnnt cnttgaaaca cacngcngaa ngttctcatt ntcccncnc caggtnaaaa 480  
 tgaagggtta ccatntttta cncacacctc acntggcnnn gcctgaatcc tcnaaaancn 540  
 cctcaancn aattnctnng ccccggtcnc gcntnngtcc cnccegggct ccgggaantn 600  
 ccccccnnga anncnntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc 660  
 cnnagactnt cctcnncnan cncaattttc ttttnttcaac gaacncgnnc cnnaaaatgn 720  
 nnnnncctc cncnngtcn naatcnccan c 751

<210> 40  
 <211> 753  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(753)  
 <223> n = A,T,C or G

<400> 40  
 gtgggtattt ctgtaagatc aggtgttcc cctcgtagg tttagaggaa acaccctcat 60  
 agatgaaaac ccccccgaga cagcagcact gcaactgcca agcagccggg gtaggagggg 120

<210> 79  
 <211> 552  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(552)  
 <223> n = A,T,C or G

<400> 79  
 tccttttgggt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg 60  
 tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt 120  
 cctctttcct ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag 180  
 tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt 240  
 atgcaagtta gtaattactc aggggttaact aaattacttt aatatgctgt tgaacctact 300  
 ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga 360  
 taatattcta tgttctaaaa gtggggctat acataaanta tnaagaaata tggaatttta 420  
 ttcccaggaa tatggggttc atttatgaat antaccggg anagaagttt tgantnaaac 480  
 cngttttggt taatacgta atagtctctn aatnaacaag gcntgactta tttccaaaaa 540  
 aaaaaaaaaa aa 552

<210> 80  
 <211> 476  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(476)  
 <223> n = A,T,C or G

<400> 80  
 acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga 60  
 ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct 120  
 cacacagact ccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt 180  
 gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtacta 240  
 aggttaaaat ttcccacca gaaaaggcaa cttagataaa atcttagagt actttcatac 300  
 tcttctaagt cctcttccag cctcactttg agtcctcctt ggggggtgat aggaantntc 360  
 tcttggtttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaat 420  
 gctgaaaaaa ttaaaatggt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa 476

<210> 81  
 <211> 232  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(232)  
 <223> n = A,T,C or G

<400> 81  
 ttttttttgg tatgcctcn ctgtgnggtt attgttgctg ccaccctgga ggagccaggt 60  
 ttcttctgta tctttctttt ctggggggtc ttcttggtc tgccttcca tcccagcct 120  
 ctcatccca tcttgcaatt ttgctagggg tggaggcgct ttcttggtag cccctcagag 180  
 actcagtcag cgggaataag tcttaggggt ggggggtgtg gcaagccggc ct 232

```

cgccctatgc acagctgggc ccttgagaca gcagggcttc gatgtcaggc tcgatgtcaa 180
tggtctggaa gcggcggctg tacctgcgta ggggcacacc gtcagggccc accaggaact 240
tctcaaagtt ccaggcaacn tcgttgcgac acaccggaga ccaggatgtn agcttgggggt 300
cggtcataaa cgcgggtggcg tcgtcgctgg gagctggcag ggcctcccg caggaggcna 360
ataaaaggtg cgcggcgca cegttcanct cgcacttctc naanaccatg angttgggct 420
cnaaccacc accannccgg acttccttga nggaattccc aaatctcttc gntcttgggc 480
ttctnctgat gccctanctg gttgccnngn atgccaanca nccccaancc cgggggtcct 540
aaanaccn cctcctentt tcatctgggt tnttntcccc ggacctggt tcctctcaag 600
gganccata tctcnaccan tactcacnt nccccccnt gnnaccanc cttctanngn 660
ttccncccg ncctctggc cntcaaan gcttnacna cctgggtctg ccttcccccc 720
tnccctatct gnacccnct tttgtctcan tnt 753

```

```

<210> 41
<211> 341
<212> DNA
<213> Homo sapien

```

```

<400> 41
actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gcttcaaattg 60
agtgaaccca tccttgattt atatacatat atgttctcag tattttggga gcctttccac 120
ttctttaaac ctgttgcatt atgaacactg aaaataggaa tttgtgaaga gtaaaaaagt 180
tatagcttgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttgag 240
tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat 300
ttttactttt tgattaattg tgttttatat attagggtag t 341

```

```

<210> 42
<211> 101
<212> DNA
<213> Homo sapien

```

```

<400> 42
acttactgaa tttagttctg tgctcttctt tatttagtgt tgtatcataa atactttgat 60
gtttcaaaca ttctaaataa ataattttca gtggcttcat a 101

```

```

<210> 43
<211> 305
<212> DNA
<213> Homo sapien

```

```

<400> 43
acatctttgt tacagtctaa gatgtgttct taaatcacca ttccttctg gtcctcacc 60
tccaggggtg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat 120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaacca 180
cctcttgaga ggtagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat 240
tggatacaga acgagagtta tcctggataa cttagagctg agtacctgcc cggggggcgc 300
tcgaa 305

```

```

<210> 44
<211> 852
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(852)
<223> n = A,T,C or G

```

```

<400> 44

```

```

acataaatat cagagaaaag tagtctttga aatatttacg tccaggagtt ctttgtttct    60
gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt    120
ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct    180
ccagaatttc tctttttag tagtatctca tagctcggtt gagcttttca taggtcatgc    240
tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga    300
agacgccctc agatcgggtc tcccatttta ttaatcctgg gttcttgtct ggggtccaaga    360
ggatgtcgcg gatgaattcc cataagttag tccctctcgg gttgtgcttt ttggtgtggc    420
acttggcagg ggggtcttgc tcctttttca tatcagggtga ctctgcaaca ggaaggtgac    480
tggtggttgt catggagatc tgagcccggc agaaagtttt gctgtccaac aaatctactg    540
tgctaccata gttggtgtca tataaatagt tctngtcttt ccagggtgtc atgatggaag    600
gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tcactactgc    660
actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg    720
ccgcccgggt gaactcctgc aaactcatgc tgcaaagggt ctcgccgttg atgtcgaaact    780
cntggaaagg gatacaattg gcatccagct ggttggtgtc caggaggtga tggagccact    840
cccacacctg gt                                     852

```

```

<210> 45
<211> 234
<212> DNA
<213> Homo sapien

```

```

<400> 45
acaacagacc cttgctcgct aacgacctca tgctcatcaa gttggacgaa tccgtgtccg    60
agtctgacac catccggagc atcagcattg cttcgcagtg ccctaccgcg gggaaactctt    120
gcctcgtttc tggctggggt ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg    180
tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgacctg ctgt       234

```

```

<210> 46
<211> 590
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (590)
<223> n = A,T,C or G

```

```

<400> 46
actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atgggtgtgta    60
atttgatagc aatatttttg agattacaga gtttttagtaa ttaccaatta cacagttaaa    120
aagaagataa tatattccaa gcanatacaa aatatctaata gaaagatcaa ggcaggaaaa    180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta    240
aaagctttca aaanaanaaa ttattgcagt ctanttaatt caaacagtgt taaatgggtat    300
caggataaan aactgaaggg canaaagaat taattttcac ttcattgtaac ncaccanant    360
ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc    420
tggtctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag    480
ggctcctggt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct    540
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt       590

```

```

<210> 47
<211> 774
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (774)
<223> n = A,T,C or G

```

```

<400> 47
acaagggggc ataatgaagg agtgggggana gatttttaaag aaggaaaaaa aacgaggccc      60
tgaacagaat ttctctgnac aacggggcctt caaaataatt ttcttgggga gggttcaagac      120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg      180
cattacagac gggactcttg gaggaaggat aaacagaaaag gggacaaaag ctaatcccaa      240
aacatcaaag aaaggaagggt ggcgtcatat cteccagcct acacagttct ccagggtctt      300
cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtgt      360
ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgtctgat cctgctggc      420
ccacactcct tgaacacaca tccccagggt atattcctgg acatggctga acctcctatt      480
cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc      540
acggcatggg aagcctttct gacttgcttg attactccag catcttggaa caatccctga      600
ttccccactc cttagaggca agataggggtg gtttaagagta gggctggacc acttgagacc      660
aggctgctgg cttcaaattt tggctcattt acgagctatg ggaccttggg caagtnatct      720
tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt          774

```

```

<210> 48
<211> 124
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(124)
<223> n = A,T,C or G

```

```

<400> 48
canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt      60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact      120
tggt                                              124

```

```

<210> 49
<211> 147
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(147)
<223> n = A,T,C or G

```

```

<400> 49
gccgatgcta ctattttatt gcaggagggt ggggtgtttt tattattctc tcaacagctt      60
tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt      120
ttagggcacc catatcccaa gcantgt                    147

```

```

<210> 50
<211> 107
<212> DNA
<213> Homo sapien

```

```

<400> 50
acattaaatt aataaaagga ctgttggggg tctgctaaaa cacatggctt gatatatattgc      60
atggtttgag gttaggagga gttaggcata tgttttggga gaggggt                    107

```

```

<210> 51
<211> 204
<212> DNA

```



<213> Homo sapien

<400> 51

gtcctaggaa	gtctagggga	cacacgactc	tgggggtcacg	gggccgacac	acttgcacgg	60
cggaaggaa	aggcagagaa	gtgacaccgt	caggggggaaa	tgacagaaaag	gaaaatcaag	120
gccttgcaag	gtcagaaaagg	ggactcaggg	cttccaccac	agccctgccc	cacttggcca	180
cctccctttt	gggaccagca	atgt				204

<210> 52

<211> 491

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(491)

<223> n = A,T,C or G

<400> 52

acaaagataa	catttatctt	ataacaaaaa	tttgatagtt	ttaaagggtta	gtattgtgta	60
gggtattttt	caaaagacta	aagagataac	tcaggtaaaa	agttagaaat	gtataaaaca	120
ccatcagaca	ggttttttaa	aaacaacata	ttacaaaatt	agacaatcat	ccttaaaaaa	180
aaaacttctt	gtatcaattt	cttttgttca	aaatgactga	cttaantatt	tttaaatttt	240
tcanaaacac	ttcctcaaaa	attttcaana	tggtagcttt	canatgtnc	ctcagtccca	300
atgttgctca	gataaataaa	tctcgtgaga	acttaccacc	caccacaagc	tttctggggc	360
atgcaacagt	gtcttttctt	tnctttttct	tttttttttt	ttacaggcac	agaaactcat	420
caattttatt	tggataacaa	agggtctcca	aattatattg	aaaaataaat	ccaagttaat	480
atcactcttg	t					491

<210> 53

<211> 484

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(484)

<223> n = A,T,C or G

<400> 53

acataattta	gcagggctaa	ttaccataag	atgctattta	ttaanaggtn	tatgatctga	60
gtattaacag	ttgctgaagt	ttggtatttt	tatgcagcat	tttctttttg	ctttgataac	120
actacagaac	ccttaaggac	actgaaaatt	agtaagtaaa	gttcagaaac	attagctgct	180
caatcaaadc	tctacataac	actatagtaa	ttaaaacggt	aaaaaaaaag	gttgaaatct	240
gcactagtat	anaccgctcc	gtcaggata	anactgcttt	ggaacagaaa	gggaaaaanc	300
agctttgant	ttctttgtgc	tgatangagg	aaaggctgaa	ttacctgtt	gcctctccct	360
aatgattggc	aggtcnggta	aatnccaaaa	catattccaa	ctcaacactt	cttttccncg	420
tancctgant	ctgtgtattc	caggancagg	cggatggaat	gggccagccc	ncggatgttc	480
cant						484

<210> 54

<211> 151

<212> DNA

<213> Homo sapien

<400> 54

actaaacctc	gtgcttgta	actccatata	gaaaacgggtg	ccatccctga	acacggctgg	60
ccactgggta	tactgctgac	aaccgcaaca	acaaaaacac	aatcccttgg	cactggctag	120

tctatgtcct ctcaagtgcc tttttgtttg t 151

<210> 55  
<211> 91  
<212> DNA  
<213> Homo sapien

<400> 55  
acctggcttg tctccgggtg gttcccggcg ccccccacgg tccccagaac ggacactttc 60  
gccctccagt ggatactcga gccaaagtgg t 91

<210> 56  
<211> 133  
<212> DNA  
<213> Homo sapien

<400> 56  
ggcggatgtg cggttggttat atacaaatat gtcattttat gtaagggact tgagtatact 60  
tggatttttg gtatctgtgg gttgggggga cgggccagga accaataccc catggatacc 120  
aagggacaac tgt 133

<210> 57  
<211> 147  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(147)  
<223> n = A,T,C or G

<400> 57  
actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc 60  
gactgggagc tgagcccttc cctttgcgcc tgcctcagag gattgttgcc gacntgcana 120  
tctcantggg ctggatncat gcagggt 147

<210> 58  
<211> 198  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(198)  
<223> n = A,T,C or G

<400> 58  
acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc 60  
tgattacata catttatcct ttaaaaaaga tgtaaatcctt aatttttatg ccatctatta 120  
atttaccaat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt 180  
ttgacttcta agtttggg 198

<210> 59  
<211> 330  
<212> DNA  
<213> Homo sapien

<400> 59

```

acaacaaatg ggttgtagg aagtcttatac agcaaaactg gtgatggcta ctgaaaagat      60
ccattgaaaa ttatcattaa tgattttaaa tgacaagtta tcaaaaactc actcaatttt      120
cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atctttctgaa      180
tacagtcaat aaatgacaaa gccagggcct acaggtgggt tccagacttt ccagacccag      240
cagaaggaaat ctattttatac acatggatct ccgtctgtgc tcaaaatacc taatgatatt      300
tttcgtcttt attggacttc tttgaagagt      330

```

```

<210> 60
<211> 175
<212> DNA
<213> Homo sapien

```

```

<400> 60
accgtgggtg ccttctacat tcttgacggc tcttcacca acatctgggt ctacttcggc      60
gtcgtgggtc ccttcctctt catcctcacc cagctgggtg tgctcatcga ctttgccgac      120
tcttgaagcc agcgttggtc gggcaaggcc gaggagtgcg attcccgtag ctggt      175

```

```

<210> 61
<211> 154
<212> DNA
<213> Homo sapien

```

```

<400> 61
accccaacttt tctcctgtg agcagctctgg acttctcact gctacatgat gagggtgagt      60
ggttggtgct cttcaacagt atcctccctt ttccggatct gctgagccgg acagcagtgc      120
tggaactgcac agccccgggg ctccacattg ctgt      154

```

```

<210> 62
<211> 30
<212> DNA
<213> Homo sapien

```

```

<400> 62
cgctcgagcc ctatagttag tcgtattaga      30

```

```

<210> 63
<211> 89
<212> DNA
<213> Homo sapien

```

```

<400> 63
acaagtcatt tcagcacctt ttgctcttca aaactgacca tcttttatat ttaatgcttc      60
ctgtatgaat aaaaatgggt atgtcaagt      89

```

```

<210> 64
<211> 97
<212> DNA
<213> Homo sapien

```

```

<400> 64
accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag      60
aatcagtgc tccaggattg gtccttggat ctgggggt      97

```

```

<210> 65
<211> 377
<212> DNA
<213> Homo sapien

```

<220>  
<221> misc\_feature  
<222> (1) ... (377)  
<223> n = A,T,C or G

<400> 65  
acaacaanaa ntcccttctt taggcactg atggaaacct ggaacccctt tttgatggca 60  
gcatggcgct ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc 120  
ccaaccctgg tctaccacaca nttctggcta tgggctgtct ctgccactga acatcagggt 180  
tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaaagt caatgagaaa 240  
ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaaccg 300  
tgggggtgaa ctaccccccag gaggaatcat gcctggggca tgcaanggtg ccaacaggag 360  
gggcgggagg agcatgt 377

<210> 66  
<211> 305  
<212> DNA  
<213> Homo sapien

<400> 66  
acgcctttcc ctcagaattc agggaagaga ctgtcgctg ccttctcccg ttgttgctg 60  
agaacccgtg tgccccctcc caccatatec accctcgctc catctttgaa ctcaaacacg 120  
aggaactaac tgcaccctgg tcctctcccc agtccccagt tcaccctcca tccctcacct 180  
tcctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt 240  
ttatatattt tttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac 300  
tggttt 305

<210> 67  
<211> 385  
<212> DNA  
<213> Homo sapien

<400> 67  
actacacaca ctccacttgc ctttgtgaga cactttgtcc cagcacttta ggaatgctga 60  
ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcagggt ctgagagttc 120  
cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180  
tgtgctgtgc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg 240  
ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300  
cctctccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgccatac 360  
catagtttct gtgctagtgg accgt 385

<210> 68  
<211> 73  
<212> DNA  
<213> Homo sapien

<400> 68  
acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa 60  
gtttttttta tgg 73

<210> 69  
<211> 536  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1) ... (536)

<223> n = A,T,C or G

<400> 69

actagtccag	tgtggtggaa	ttccattgtg	ttggggggtc	tcaccctcct	ctcctgcagc	60
tccagctttg	tgctctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
cccggtgtgc	atctataacg	cagacctcaa	tgatgagtgg	gtacagcgtg	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgtc	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttcttcgacg	tagaggtggg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttggacacc	tgtgccttcc	atgaacagcc	420
agaactgcag	aagaaacagt	tgtgctcttt	cgagatctac	gaagttccct	ggggagaaca	480
gaangtcctt	gggtgaaatc	caggtgtcaa	gaaatcctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgaccccta	acagggggccc	tctcagccct	cctaatagacc	tccggcctag	ccatgtgatt	60
tcacttccac	tccataacgc	tctcataact	aggcctacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggc	cttcgatacg	ggataatcct	atttattacc	tcagaagttt	ttttcttcgc	240
agggattttt	ctgagccttt	taccactcca	gcctagcccc	taccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgctaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgtattact	cgcatacagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctattttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattggttta	120
tgtgatttta	gtggtatttt	tggcaccctt	atatatgttt	tccaaacttt	cagcagtgat	180
attattttcca	taacttaaaa	agtgagtttg	aaaaagaaaa	tctccagcaa	gcattctcatt	240
taaataaaagg	tttgtcatct	ttaaaaatac	agcaatatgt	gactttttta	aaaagctgtc	300
aaataggtgt	gacctacta	ataattatta	gaaatacatt	taaaaacatc	gagtacctca	360
agtcagtttg	ccttgaaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tattttttaa	aagtacatgg	480
taaaaaaaaa	aattcacaac	agtatataag	gctgtaaaaa	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(511)

<223> n = A,T,C or G

```

<400> 72
tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcggtgta      60
aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa      120
aagccgcagg atgtctacac tatancaggc gctatctggg ttggctggag gagctgtgga      180
aaacatggan agattggtgc tgganatcgc cgtggctatt cctcattggt attacanagt      240
gagggttctct gtgtgcccac tggtttgaaa accgttctnc aataatgata gaatagtaca      300
cacatgagaa ctgaaatggc ccaaaccacg aaagaaagcc caactagatc ctcagaanac      360
gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgcccc gtctgttatg      420
atctctctcc attgcagcna naaaccggtt cttctaagca aacncagggt atgatggcna      480
aaatacaccc cctcttgaag naccnggagg a                                     511

```

```

<210> 73
<211> 499
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(499)
<223> n = A,T,C or G

```

```

<400> 73
cagtgccagc actggtgcca gtaccagtac caataacagt gccagtgcc gtgccagcac      60
cagtgggtggc ttcagtgtct gtgccagcct gaccgccact ctcacatttg ggctcttcgc      120
tggccttgggt ggagctgggt ccagcaccag tggcagctct ggtgcctgtg gtttctccta      180
caagtgaagt tttagatatt gttaatcctg ccagtcttct tcttcaagcc aggggtgcac      240
ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagtgtaca      300
ctctgcatta aatctatttg ccatttctga aaaaaaaaaa aaaaaaaggg cggccgctcg      360
antctagagg gcccgtttaa acccgctgat cagcctcgac tgtgccttct anttgccagc      420
catctgttgt ttgcccctcc cccgntgcct tccttgacct tggaaagtgc cactcccact      480
gtcctttcct aantaaaaa                                     499

```

```

<210> 74
<211> 537
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(537)
<223> n = A,T,C or G

```

```

<400> 74
tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat      60
ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact      120
tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa      180
cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga      240
aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag      300
ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc      360
cagtttgctt gatataattg ttgatattaa gattcttgac ttataatttg aatgggttct      420
actgaaaaan gaatgatata ttcttgaaga catcgatata cattatttta cactcttgat      480
tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtccccgt      537

```

```

<210> 75
<211> 467
<212> DNA
<213> Homo sapien

```

<220>  
 <221> misc\_feature  
 <222> (1)...(467)  
 <223> n = A,T,C or G

<400> 75  
 caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc 60  
 tgcattattac acgtacctcc tctgtctcct caagtagtgt ggtctatttt gccatcatca 120  
 cctgtctgtc gcttagaaga acggccttct gctgcaangg agagaaatca taacagacgg 180  
 tggcacaagg aggccatctt ttccctcatcg gttattgtcc ctagaagcgt cttctgagga 240  
 tctagttggg ctttctttct gggtttgggc catttcantt ctcattgtgt tactattcta 300  
 tcattattgt ataacgggtt tcaaaccngt gggcacncag agaacctcac tctgtaataa 360  
 caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc 420  
 ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(400)  
 <223> n = A,T,C or G

<400> 76  
 aagctgacag cattcgggccc gagatgtctc gctccgtggc cttagctgtg ctgcgcgtac 60  
 tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc 120  
 atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg tttcatccat 180  
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag 240  
 acttgtcttt cagcaaggac tggctcttct atctcttgta ctacactgaa ttcaccccca 300  
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360  
 tttagtgagg taanacatg taagcagcan catgggaggt 400

<210> 77  
 <211> 248  
 <212> DNA  
 <213> Homo sapien

<400> 77  
 ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60  
 ccagctgccc cggcggggga tgcgaggtcc ggagcaccct tgcccggctg tgattgctgc 120  
 caggcactgt tcatctcagc ttttctgtcc ctttgtctcc ggcaagcgtc tctgtctgaa 180  
 gttcatatct ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaa 240  
 aaaaaaaa 248

<210> 78  
 <211> 201  
 <212> DNA  
 <213> Homo sapien

<400> 78  
 actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca 60  
 tccccagac cccgccttgc ccgtgcccc cgtgctgtgt aacgacagta tgatgcttac 120  
 tctgtacttc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataatgcct 180  
 gatttaaaaa aaaaaaaaaa a 201

<210> 82  
 <211> 383  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(383)  
 <223> n = A,T,C or G

<400> 82  
 aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactgggtgcc 60  
 agtaccagta ccaataacat gccagtgccca gtgccagcac cagtgggtggc ttcagtgtctg 120  
 gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggt ggagctgggtg 180  
 ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtggatg tttagatatt 240  
 gttaatcctg ccagtctttc tcttcaagcc aggggtgcac ctcagaaacc tactcaacac 300  
 agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg 360  
 ccatttcaaa aaaaaaaaaa aaa 383

<210> 83  
 <211> 494  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(494)  
 <223> n = A,T,C or G

<400> 83  
 accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca 60  
 gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgctcagc 120  
 ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa 180  
 acgcttcaag gtgctcatga cccagcaacc gcgcctgtc ctctgagggg ccttaaactg 240  
 atgtcttttc tgccacctgt taccctctcg agactccgta accaaactct tcggactgtg 300  
 agccctgatg ccttttttgc agccatactc tttggentcc agtctctcgt ggcgattgat 360  
 tatgcttgtg tgaggcaatc atgggtggcat caccatnaa gggaacacat ttganttttt 420  
 tttncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta 480  
 aaaaaaaaaa aaaa 494

<210> 84  
 <211> 380  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(380)  
 <223> n = A,T,C or G

<400> 84  
 gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca 60  
 agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattcccag 120  
 gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg 180  
 gcacaccctc ctggggccca ggagggcacc tgcgtctccc agtatgccaa ctggctgggtg 240  
 gtgctgtctc tegtcatctt cctgctcgtg gccaacatcc tgctgggtcac ttgctcattg 300  
 ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360  
 agcgttnccg cctcatccgg 380



<210> 85  
 <211> 481  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(481)  
 <223> n = A,T,C or G

<400> 85  
 gagttagctc tccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60  
 tnccatcgct atactgtagg ttgcccacca cctcctgcat cttggggcgg ctaatatcca 120  
 ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180  
 tgtgaaagga tctccagaag gagtgtctga tcttccccac acttttgatg actttattga 240  
 gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtgag gtcaccagcc 300  
 ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360  
 ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggnngaa 420  
 aaagaacacc tcttggaagt gctngccgct cctcgtccnt tgggtggnngc gcntnccttt 480  
 t 481

<210> 86  
 <211> 472  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(472)  
 <223> n = A,T,C or G

<400> 86  
 aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60  
 acttggaaaa gcaacttnaa gcttggacac tggattataa attcacaata tgcaacactt 120  
 taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180  
 ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240  
 cacaagtcgg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt 300  
 catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360  
 atatntgagc ggaagantag cctttctact tcaccagaca caactccttt catattggga 420  
 tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

<210> 87  
 <211> 413  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(413)  
 <223> n = A,T,C or G

<400> 87  
 agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaatTT tgtgtgcgtg 60  
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 cctcttttgg atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180  
 ttgtcttctg tgtaaagtgt actagagaaa acacctatnt tatgagtcaa tctagttngt 240  
 tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg 300

```

ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctgggtgaga aattncataa 360
acagaaattg ggtngtatat tgaaanannng catcattnaa acgttttttt ttt 413

```

```

<210> 88
<211> 448
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(448)
<223> n = A,T,C or G

```

```

<400> 88
cgcagcgggt cctctctatc tagctccage ctctcgctg cccactccc cgcgtcccgc 60
gtcctagcnn accatggccg ggcccctgcg cgcccgcgtg ctctgctgg ccacccctggc 120
cgtggccctg gccgtgagcc cgcggcccg ctccagtcgc ggcaagccgc cgcgcctggg 180
gggaggccca tggaccccgc gtggaagaag aagggtgctg gcgtgcactg gactttgccg 240
tcggcnanta caacaaaccc gcaacnactt ttaccnagen cgcgctgcag gttgtgccgc 300
cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng 360
tttaccagaa ccnagccaat tngaacaatt nccccccat aacagcccct tttaaaaagg 420
gaancantcc tgntcttttc caaat ttt 448

```

```

<210> 89
<211> 463
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(463)
<223> n = A,T,C or G

```

```

<400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca 60
gtagtgatcc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc 120
agaggtctag gtctgcatat cagcagacag ttgtgccgtg tattttgtag ccttgaagtt 180
ctcagtgaca agttnnntct gatgcgaagt tctnattcca gtgttttagt cctttgcac 240
tttnatgttn agacttgccct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg 300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn 360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn 420
aattcnana anttcagntn tcatacaaca naacngganc ccc 463

```

```

<210> 90
<211> 400
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(400)
<223> n = A,T,C or G

```

```

<400> 90
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cttcactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaat 120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttcact 180
tcctttgtta agacttcac tggtaaagtc ttaagttttg tagaaaggaa ttaattgct 240

```

cgttctctaa	caatgtcctc	tccttgaagt	atttggtga	acaaccacc	tnaagtcct	300
ttgtgcatcc	attttaata	tacttaata	ggcattggn	cactaggta	aattctgcaa	360
gagtcactcg	tctgcaaaag	ttgcgttagt	atatctgcca			400

<210> 91  
 <211> 480  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (480)  
 <223> n = A,T,C or G

<400> 91						
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atgcctcttt	gactaccgtg	tgccagtgtt	ggtgattctc	acacacctcc	nnccgctctt	180
tgtggaaaaa	ctggcacttg	nctggaaacta	gcaagacatc	acttacaagt	tcacccacga	240
gacacttgaa	aggtgtaaca	aagcgactct	tgcattgctt	tttgtccctc	cggcaccagt	300
tgtcaatact	aaccgctggg	tttgcttcca	tcacatttgt	gatctgtagc	tctggatata	360
tctcctgaca	gtactgaaga	acttcttctt	ttgtttcaaa	agcaactctt	ggtgcctgtt	420
ngatcagggt	cccatttccc	agtccgaatg	ttcacatggc	atatnttact	tcccacaaaa	480

<210> 92  
 <211> 477  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (477)  
 <223> n = A,T,C or G

<400> 92						
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cccagcgagg	cagcagcggg	gccggtcaat	gaactccact	cgtggcttgg	ggttgacggt	180
taantgcagg	aagaggctga	ccacctcgcg	gtccaccagg	atgcccgaact	gtgcgggacc	240
tgcagcgaaa	ctcctcgatg	gtcatgagcg	ggaagcgaat	gangcccagg	gccttgccca	300
gaaccttccg	cctgttctct	ggcgtcacct	gcagctgctg	ccgctnacac	tcggcctcgg	360
accagcgagc	aaacggcggt	gaacagccgc	acctcacgga	tgcccantgt	gtcgcgctcc	420
aggaacggcn	ccagcgtgtc	caggtcaatg	tcggtgaanc	ctccgcgggt	aatggcg	477

<210> 93  
 <211> 377  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (377)  
 <223> n = A,T,C or G

<400> 93						
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agtcggagca	gccccagacc	gctgccgccc	gaagctaagc	ctgcctctgg	ccttcccctc	120
cgctcgaatg	cagaaccant	agtgaggagca	ctgtgttttag	agttaagagt	gaacactgtn	180

tgatcttact	tggaatttc	ctctgttata	tagcttttcc	caatgcta	ttccaaacaa	240
caacaacaaa	ataacatgtt	tgctgttna	gttgataaaa	agtangtgat	tctgtatnta	300
aagaaaatat	tactgttaca	tatactgctt	gcaanttctg	tatttattgg	tnctctggaa	360
ataaatatat	tattaaa					377

<210> 94  
 <211> 495  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(495)  
 <223> n = A,T,C or G

<400> 94						
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ccaaggaaag	accaccttct	ggggacatgg	gctggagggc	aggacctaga	ggcaccaagg	180
gaaggcccca	ttccggggct	gttccccgag	gaggaaggga	aggggctctg	tgtgcccccc	240
acgaggaana	ggccctgant	cctgggatca	nacaccctt	cacgtgtatc	cccacacaaa	300
tgcaagctca	ccaagggtccc	ctctcagtc	cttccctaca	ccctgaacgg	ncactggccc	360
acaccacccc	agancancca	cccgccatgg	ggaatgttct	caaggaatcg	cngggcaacg	420
tggaactctng	ttccnnaagg	gggcagaatc	ttcaatagan	gganngaacc	cttgctnana	480
aaaaaaaaana	aaaaa					495

<210> 95  
 <211> 472  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(472)  
 <223> n = A,T,C or G

<400> 95						
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cctctggaag	ccttgcgag	agcggacttt	gtaattgttg	gagaataact	gctgaatttt	120
tagctgtttt	gagttgattc	gcaccactgc	accacaactc	aatatgaaaa	ctatttnact	180
tatttattat	cttgtgaaaa	gtatacaatg	aaaattttgt	tcatactgta	tttatcaagt	240
atgatgaaaa	gcaatagata	tatattcttt	tattatgttn	aattatgatt	gccattatta	300
atcggcaaaa	tgtggagtgt	atgttctttt	cacagtaata	tatgcctttt	gtaacttcac	360
ttggttattt	tattgtaaat	gaattacaaa	attcttaatt	taagaaaatg	gtangttata	420
tttanttcan	taatttcttt	ccttgtttac	gttaattttg	aaaagaatgc	at	472

<210> 96  
 <211> 476  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(476)  
 <223> n = A,T,C or G

<400> 96						
ctgaagcatt	tcttcaaact	tntctacttt	tgctattgat	acctgtagta	agttgacaat	60

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```

<210> 97

<211> 479

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(479)

<223> n = A,T,C or G

<400> 97

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actctttcta atgctgatat gatcttgagt ataagaatgc atatgtcact agaatggata 60
aaataatgct gcaaaacttaa tgttcttatg caaaatggaa cgctaataa acacagctta 120
caatcgcaaa tcaaaactca caagtgtcct tctgttgtag atttagtgta ataagactta 180
gattgtgctc cttcgatat gattgtttct canatcttg gcaatnttcc ttagtcaa at 240
caggctacta gaattctgtt attggatatn tgagagcatg aaatttttaa naatacactt 300
gtgattatna aattaatcac aaatttcact tatacctgct atcagcagct agaaaaacat 360
ntnnttttta natcaaagta ttttgtgttt ggaantgttn aaatgaaatc tgaatgtggg 420
ttcnatctta ttttttccn gacnactant tnccttttta gggncctatc tganccatc 479

```

<210> 98

<211> 461

<212> DNA

<213> Homo sapien

<400> 98

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agtgacttgt cctccaacaa aacccttgga tcaagtttgt ggcaactgaca atcagaccta 60
tgctagtctc tgctcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca 120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga 180
agtgattcag ttctctctac ggatgagaga ctggctcaag aatatactca tgcagcttta 240
tgaagccact ctgaacacgc tggttatcta gatgagaaca gagaaataaa gtcagaaaat 300
ttacctggag aaaagaggct ttggctgggg accatcccat tgaaccttct cttaaggact 360
ttaagaaaaa ctaccacatg ttgtgtatcc tgggtccggc cgtttatgaa ctgaccacc 420
tttggaataa tcttgacgct cctgaacttg ctcctctgcg a 461

```

<210> 99

<211> 171

<212> DNA

<213> Homo sapien

<400> 99

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gtggcgcgc gcaggtgttt cctcgtagcg cagggccccc tcccttcccc aggcgtccct 60
cggcgctct gcgggccga ggaggagcgg ctggcgggtg gggggagtgt gaccaccct 120
cggtgagaaa agccttctct agcgatctga gaggcgtgcc ttgggggtac c 171

```

<210> 100

<211> 269

<212> DNA

<213> Homo sapien

&lt;400&gt; 100

cgggccgcaag	tgcaactcca	gctggggccg	tgcgagacgaa	gattctgccca	gcagttgggc	60
cgactgcgac	gacggcggcg	gcgacagtcg	caggtgcagc	gcggggcgct	ggggtcttgc	120
aaggctgagc	tgacgccgca	gaggtcgtgt	cacgtcccac	gaccttgacg	ccgtcgggga	180
cagccggaac	agagcccgtt	gaagcgggag	gcctcgggga	gcccctcggg	aagggcggcc	240
cgagagatac	gcaggtgcag	gtggccgcc				269

&lt;210&gt; 101

&lt;211&gt; 405

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 101

tttttttttt	ttttggaatc	tactgcgagc	acagcaggtc	agcaacaagt	ttattttgca	60
gctagcaagg	taacagggtg	gggcatgggt	acatgttcag	gtcaacttcc	tttgtcgtgg	120
ttgattgggt	tgtctttatg	ggggcggggg	ggggtagggg	aaacgaagca	aataacatgg	180
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ctgtttctgga	gggagattag	ggtttcttgc	caaattccaac	aaaatccact	gaaaaagttg	360
gatgatcagt	acgaataaccg	aggcatattc	tcatatcggg	ggcca		405

&lt;210&gt; 102

&lt;211&gt; 470

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 102

tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	60
ggcacttaat	ccatttttat	ttcaaaatgt	ctacaaattt	aatcccatta	tacgggtattt	120
tcaaaatcta	aattattcaa	attagccaaa	tccttaccaa	ataataccca	aaaatcaaaa	180
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&lt;210&gt; 103

&lt;211&gt; 581

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 103

tttttttttt	ttttttttga	ccccctctt	ataaaaaaca	agttaccatt	ttatttttact	60
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agggaaaaaca	ggaagagaaa	tggcacacaa	aacaaacatt	ttatattcat	atttctacct	420
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&lt;210&gt; 104

&lt;211&gt; 578

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 104

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&lt;210&gt; 105

&lt;211&gt; 538

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 105

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&lt;210&gt; 106

&lt;211&gt; 473

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 106

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&lt;210&gt; 107

&lt;211&gt; 1621

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 107

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agttattctg ccttccagtt tgcttgatat atttgttgat attaagattc ttgacttata 1440
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aaaagtcacg tgaacaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620
a

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&lt;210&gt; 108

&lt;211&gt; 382

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 108

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Met Ala Leu Gln Gly Ile Ser Val Met Glu Leu Ser Gly Leu Ala Pro
1 5 10 15
Gly Pro Phe Cys Ala Met Val Leu Ala Asp Phe Gly Ala Arg Val Val
20 25 30
Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
35 40 45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50 55 60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65 70 75 80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85 90 95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100 105 110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115 120 125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130 135 140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145 150 155 160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165 170 175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180 185 190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195 200 205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg
210 215 220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe
225 230 235 240
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
245 250 255

```



Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala  
 260 265 270  
 Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp  
 275 280 285  
 Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val  
 290 295 300  
 His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu  
 305 310 315 320  
 Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Asn Thr Pro Ala  
 325 330 335  
 Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu  
 340 345 350  
 Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn  
 355 360 365  
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 370 375 380

<210> 109  
 <211> 1524  
 <212> DNA  
 <213> Homo sapien

<400> 109  
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 cagtgcgacc tagtggtctt cacctgcttc ctcttgggcg tgggctgccg gctgaccccg 180  
 ggtttgtacc acctggggcg cactgtcttc tgcctcgact tcatggtttt cacgggtgcgg 240  
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 gtcttctacc gtccctacct gcagatcttc gggcagattc ccaggagga catggacgtg 480  
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 ccacagggga ttttgtcctt agagtaaggc tcatctgggc ctcgccccc gcacctgggtg 1260  
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 cagaggaaaa aaaaaaaaaa aaaa 1524

<210> 110  
 <211> 3410  
 <212> DNA  
 <213> Homo sapien

<400> 110  
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aaaaaaaaara	aaaaaaaaaa	aaaaaaaaaa	aaaaaaataa	aaaaaaaaaa		3410

&lt;210&gt; 111

&lt;211&gt; 1289

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 111

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agccaggcgt ccctctgect gccactcag tggcaacacc cgggagctgt tttgtccttt      60
gtggagcctc agcagttccc tctttcagaa ctcactgcca agagccctga acaggagcca      120
ccatgcagtg cttcagcttc attaagacca tgatgatcct cttcaatttg ctcactcttc      180
tgtgtggtgc agccctggtg gcagtgggca tctgggtgtc aatcgatggg gcactccttc      240
tgaagatctt cgggccactg tcgtccagtg ccatgcagtt tgtcaacgtg ggctacttcc      300
tcacgcgagc cggcgttggt gtctttgtct ttggtttcct gggctgctat ggtgctaaga      360
ctgagagcaa gtgtgccctc gtgacgttct tcttcactct cctcctcatc ttcattgctg      420
aggttgacgc tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt      480
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ccaacacagc caatgaaacc tgcaccaagc aaaaggctca cgacaaaaaa gtagagggtt      720
gcttcaatca gcttttgtat gacatccgaa ctaatgcagt caccgtgggt ggtgtggcag      780
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atgcctgact ttccttccat tgggtgggtg atgggtgggg ggcattccag agcctctaag      1080
gtagccagtt ctgttgccca tccccccagt ctattaaacc cttgatatgc cccctaggcc      1140
tagtggtgat cccagtgtc tactggggga tgagagaaag gcattttata gcctgggcat      1200
aagtgaatc agcagagcct ctgggtggat gtgtagaagg cacttcaaaa tgcataaacc      1260
tgttacaatg ttaaaaaaaaa aaaaaaaaaa                                     1289

```

&lt;210&gt; 112

&lt;211&gt; 315

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 112

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Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln
 1          5          10          15
Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe
 20          25          30
Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
 35          40          45
Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
 50          55          60
Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
 65          70          75          80
Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
 85          90          95
Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
100          105          110
Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Val Ile Phe
115          120          125
Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe
130          135          140
Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys
145          150          155          160
Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu
165          170          175
Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln
180          185          190
Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu

```

195	200	205
His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr		
210	215	220
Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp		
225	230	235
Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val		240
	245	250
Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg		255
	260	265
Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly		270
	275	280
Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly		285
	290	295
Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp		300
305	310	315

&lt;210&gt; 113

&lt;211&gt; 553

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 113

Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala		
1	5	10
Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu		15
	20	25
Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val		30
	35	40
Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly		45
	50	55
Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly		60
65	70	75
Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile		80
	85	90
Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu		95
	100	105
Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly		110
	115	120
Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu		125
	130	135
Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala		140
145	150	155
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr		160
	165	170
Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu		175
	180	185
Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu		190
	195	200
Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly		205
	210	215
Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His		220
225	230	235
Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu		240
	245	250
Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg		255
	260	265
Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe		270
	275	280
		285

Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val  
 290 295 300  
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
 305 310 315 320  
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu  
 325 330 335  
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg  
 340 345 350  
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala  
 355 360 365  
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu  
 370 375 380  
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala  
 385 390 395 400  
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly  
 405 410 415  
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu  
 420 425 430  
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala  
 435 440 445  
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser  
 450 455 460  
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala  
 465 470 475 480  
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp  
 485 490 495  
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser  
 500 505 510  
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala  
 515 520 525  
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp  
 530 535 540  
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
 545 550

&lt;210&gt; 114

&lt;211&gt; 241

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 114

Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu  
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 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val  
 20 25 30  
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser  
 35 40 45  
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly  
 50 55 60  
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr  
 65 70 75 80  
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile  
 85 90 95  
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr  
 100 105 110  
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys  
 115 120 125  
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met

130		135		140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp				
145		150	155	160
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn				
	165		170	175
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala				
	180		185	190
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile				
	195	200	205	
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly				
	210	215	220	
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu				
225		230	235	240
Gln				

<210> 115  
 <211> 366  
 <212> DNA  
 <213> Homo sapien

<400> 115  
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 ttggtttggt aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180  
 actggtagaa aaacatctga agagctagtc tatcagcatc tgacagggtga attggatggt 240  
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300  
 tctctacatg cataacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt 360  
 ttagtc 366

<210> 116  
 <211> 282  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(282)  
 <223> n = A,T,C or G

<400> 116  
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 gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa 120  
 agactttact attttcatat ttaagacac atgatttata ctattttagt aacctgggtc 180  
 atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt 240  
 tcaatctnga actatctana tcacagacat ttctattcct tt 282

<210> 117  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(305)  
 <223> n = A,T,C or G

<400> 117

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aataaggcaa aatatatgaa acaacagggtc tcgagatatt ggaaatcagt caatgaagga      180
tactgatccc tgatcactgt cctaattgcag gatgtgggaa acagatgagg tcacctctgt      240
gactgcccca gcttactgcc thtagagagt ttctangctg cagttcagac agggagaaat      300
tggtg      305

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<210> 118
<211> 71
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(71)
<223> n = A,T,C or G

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<400> 118
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aantcctggg t      71

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<210> 119
<211> 212
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(212)
<223> n = A,T,C or G

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<400> 119
actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca      60
gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac      120
agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant      180
aatggantca aganactccc aggcctcagc gt      212

```

```

<210> 120
<211> 90
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(90)
<223> n = A,T,C or G

```

```

<400> 120
actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggctcttgcc      60
ctccgccggc gcagaacatg ctgggggtggt      90

```

```

<210> 121
<211> 218
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```

<222> (1)...(218)

<223> n = A,T,C or G

<400> 121

tgtancgtga	anacgacaga	nagggttgtc	aaaaatggag	aanccttgaa	gtcattttga	60
gaataagatt	tgctaaaaga	tttggggcta	aaacatgggt	attgggagac	atttctgaag	120
atatncangt	aaattangga	atgaattcat	ggttcttttg	ggaattcctt	tacgatngcc	180
agcatanact	tcatgtgggg	atancagcta	cccttgta			218

<210> 122

<211> 171

<212> DNA

<213> Homo sapien

<400> 122

taggggtgta	tgcaactgta	aggacaaaaa	ttgagactca	actggcttaa	ccaataaagg	60
catttgtag	ctcatggaac	aggaagtcgg	atgggtgggc	atcttcagt	ctgcatgagt	120
caccaccccg	gcgggggtcat	ctgtgccaca	ggccctgtt	gacagtgcgg	t	171

<210> 123

<211> 76

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(76)

<223> n = A,T,C or G

<400> 123

tgtagcgtga	agacnacaga	atgggtgtgtg	ctgtgctatc	caggaacaca	tttattatca	60
ttatcaanta	ttgtgt					76

<210> 124

<211> 131

<212> DNA

<213> Homo sapien

<400> 124

acctttcccc	aaggccaatg	tcctgtgtgc	taactggccg	gctgcaggac	agctgcaatt	60
caatgtgctg	ggatcatatg	aggggaggag	actctaaaat	agccaatttt	attctcttgg	120
ttaagatttg	t					131

<210> 125

<211> 432

<212> DNA

<213> Homo sapien

<400> 125

actttatcta	ctggctatga	aatagatgg	ggaaaattgc	gttaccaact	ataccactgg	60
cttgaaaaag	aggtgatagc	tcttcagagg	acttgtgact	tttgctcaga	tgctgaagaa	120
ctacagtctg	catttggcag	aaatgaagat	gaatttggat	taaatgagga	tgctgaagat	180
ttgectcacc	aaacaaaagt	gaaacaactg	agagaaaatt	ttcaggaaaa	aagacagtgg	240
ctcttgaaat	atcagtcact	tttgagaatg	ttcttagtt	actgcatact	tcatggatcc	300
catgggtggg	gtcttgcatc	tgtaagaatg	gaattgattt	tgcttttgca	agaatctcag	360
caggaaacat	cagaaccact	atcttctagc	cctctgtcag	agcaaaccct	agtgcctctc	420
ctctttgctt	gt					432



<210> 126  
 <211> 112  
 <212> DNA  
 <213> Homo sapien

<400> 126  
 acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60  
 agtaagaatg atatttcccc ccagggatca ccaaattttt ataaaaattt gt 112

<210> 127  
 <211> 54  
 <212> DNA  
 <213> Homo sapien

<400> 127  
 accacgaaac cacaacaag atggaagcat caatccactt gccaaagcaca gcag 54

<210> 128  
 <211> 323  
 <212> DNA  
 <213> Homo sapien

<400> 128  
 acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60  
 acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120  
 ttctctctga agtctagggtt acccattttg gggaccatt ataggcaata aacacagttc 180  
 ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt 240  
 ttcttgcaaa aggctcactc agtcccttgc ttgtcagtg gactgggctc cccagggcct 300  
 aggtgcctt cttttccatg tcc 323

<210> 129  
 <211> 192  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(192)  
 <223> n = A,T,C or G

<400> 129  
 acatacatgt gtgtatatatt ttaaatatca cttttgtatc actctgactt ttttagcatc 60  
 tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120  
 tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg 180  
 gataaacaac gt 192

<210> 130  
 <211> 362  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(362)  
 <223> n = A,T,C or G

<400> 130  
 ccctttttta tggatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca 60

```

tataatgacg caacaaaaag gtgctgttta gtcctatggt tcagtttatg cccctgacaa 120
gtttccattg tgttttgccg atcttctggc taatcgtggt atcctccatg ttattagtaa 180
ttctgtattc cattttgtta acgcctggta gatgtaacct gctangaggc taactttata 240
cttatttaaa agctcttatt ttgtggcat taaaatggca atttatgtgc agcactttat 300
tgcagcagga agcacgtgtg ggttggttgt aaagctcttt gctaactcta aaaagtaatg 360
gg 362

```

```

<210> 131
<211> 332
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (332)
<223> n = A,T,C or G

```

```

<400> 131
ctttttgaaa gatcgtgtcc actcctgtgg acatcttgtt ttaatggagt tcccatgca 60
gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaatgaga 120
gttctcccag gtctgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc 180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttggtttatt atccaactaa 240
cttccatctg ttatcactgg agaaagccca gactccccan gacnggtacg gattgtgggc 300
atanaaggat tgggtgaagc tggcgttgtg gt 332

```

```

<210> 132
<211> 322
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (322)
<223> n = A,T,C or G

```

```

<400> 132
acttttgcca ttttgtatat ataaacaatc ttgggacatt ctctgaaaa ctaggtgtcc 60
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat 120
ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggaccttg tatctcgggt 180
tttagcaagt taaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg 240
ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaagcct 300
gtaacaatct acaattgggt ca 332

```

```

<210> 133
<211> 278
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (278)
<223> n = A,T,C or G

```

```

<400> 133
acaagccttc acaagtttaa ctaaattggg attaattctt ctgtanttat ctgcataatt 60
cttggttttc ttccatctg gtcctgggt tgacaatttg tggaaacaac tctattgcta 120
ctattttaaa aaaatcaca atctttccct ttaagctatg ttnaattcaa actattcctg 180
ctattcctgt ttgtgcaaag aaattatatt tttcaaaata tgtntatttg ttgtatgggt 240

```

cccacgaaac actaataaaaa accacagaga ccagcctg 278

<210> 134

<211> 121

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(121)

<223> n = A,T,C or G

<400> 134

gtttanaaaa cttgttttagc tccatagagg aaagaatggt aaactttgta ttttaaaaca 60  
tgattctctg aggttaaact tggttttcaa atgttatatt tacttgtatt ttgcttttgg 120  
t 121

<210> 135

<211> 350

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(350)

<223> n = A,T,C or G

<400> 135

acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc 60  
atancaagtg gtgactgggt aagcgtgcga caaaggctag ctggcacatt acttgtgtgc 120  
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtaactcca 180  
gggtgcccc caactoctgc agccgctoct ctgtgccagn ccctgnaagg aactttcgct 240  
ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgctgag 300  
ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt 350

<210> 136

<211> 399

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(399)

<223> n = A,T,C or G

<400> 136

tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccaggggt 60  
gctgtgattg tatccgaata ntcctcgtga gaaaagataa tgagatgacg tgagcagcct 120  
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga 180  
cctggcgccc agccagccag ccacaggtgg gcttcttctt tttgtggtga caacnccaag 240  
aaaactgcag agggccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtgc 300  
tcccaggaac ccgggcaaag gccatcccca cctacagcca gcatgcccac tggcgtgatg 360  
ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

<210> 137

<211> 165

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(165)  
 <223> n = A,T,C or G

<400> 137  
 actggtgtgg tngggggtga tgctggtggg anaagttgan gtgacttcan gatggtgtgt 60  
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120  
 ttggctgggc ccactggtgg tcactgtcat tgggtggggtt cctgt 165

<210> 138  
 <211> 338  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(338)  
 <223> n = A,T,C or G

<400> 138  
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60  
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa 120  
 tgctgggcag tctcccatgc cttccacagt gaaagggtt gagaaaaatc acatccaatg 180  
 tcatgtgttt ccagccacac caaaagggtgc ttggggtgga gggctggggg catananggt 240  
 cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa 300  
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139  
 <211> 382  
 <212> DNA  
 <213> Homo sapien

<400> 139  
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60  
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccga gtgaaggaga 120  
 attcaaacag acctcgtcat tcctggtgtg agcctggtcg gctcaccgcc tatcatctgc 180  
 atttgcccta ctccagggtct accggactct ggccctgat gtctgtagt ttacaggatg 240  
 ccttattttg cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat 300  
 gtcagctatg tgccccatcc tccttcatgc cctccctccc tttcctacca ctgctgagt 360  
 gcctggaact tgtttaaagt gt 382

<210> 140  
 <211> 200  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(200)  
 <223> n = A,T,C or G

<400> 140  
 accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat 60  
 acttttcatt taacancttt tgtaagtgt caggctgcac ttgctccat anaattattg 120  
 ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt 180  
 atattcagca taaaggagaa 200

<210> 141  
 <211> 335  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(335)  
 <223> n = A,T,C or G

<400> 141  
 actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg 60  
 ggggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc aggggttggt 120  
 atgcatgtag agaaccctaaa ctaattttatt aaacaggata gaaacaggct gtctgggtga 180  
 aatgggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240  
 tttttctacc agttcagaga tnggttaatg actanttcca atggggaaaa agcaagatgg 300  
 attcacaac caagtaattt taaacaaaga cactt 335

<210> 142  
 <211> 459  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(459)  
 <223> n = A,T,C or G

<400> 142  
 accagggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta 60  
 ggggtgtttaa aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat 120  
 ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca 180  
 cacatgggtcc aacaacactc aaataataaa tcaaataatna tcagatgtta aagattggtc 240  
 ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca 300  
 tcaacacetc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga 360  
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420  
 cagcangggg gggaggaacc agtcaacct tggcgant 459

<210> 143  
 <211> 140  
 <212> DNA  
 <213> Homo sapien

<400> 143  
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60  
 aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag 120  
 accatccgac ttccctgtgt 140

<210> 144  
 <211> 164  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(164)  
 <223> n = A,T,C or G

```

<400> 144
acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct    60
atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg    120
aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt                    164

```

```

<210> 145
<211> 303
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

```

```

<400> 145
acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa    60
actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat    120
gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca    180
gtagggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag    240
tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat    300
caa                                                    303

```

```

<210> 146
<211> 327
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(327)
<223> n = A,T,C or G

```

```

<400> 146
actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac    60
actggcctgg agtgactcat tgctctgggt ggttgagaga gctcctttgc caacaggcct    120
ccaagtcagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt    180
cctgaacagg gagggtgga ggagccagca tggaaacaagc tgccactttc taaagtagcc    240
agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg    300
taggggtgag ctgtgtgact ctatggt                    327

```

```

<210> 147
<211> 173
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(173)
<223> n = A,T,C or G

```

```

<400> 147
acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg    60
actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt    120
atattcaagc acatatgtta tatattatc agttccatgt ttatagccta gtt                    173

```

```

<210> 148

```

<211> 477  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(477)  
 <223> n = A,T,C or G

<400> 148  
 acaaccactt tatctcatcg aattttttaac ccaaactcac tcactgtgcc tttctatcct 60  
 atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact 120  
 gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg 180  
 gtgggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgctcac 240  
 nccancccaac ctacccgacc ccacccctctt acacagctac ctccttgctc tetaacccca 300  
 tagattatnt ccaaattcag tcaattaagt tactattaac actctaccgg acatgtccag 360  
 caccactggg aagccttctc cagccaacac acacacacac acacncacac acacacatat 420  
 ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atgggtgg 477

<210> 149  
 <211> 207  
 <212> DNA  
 <213> Homo sapien

<400> 149  
 acagttgtat tataatatca agaaataaac ttgcaatgag agcattttaag agggaagaac 60  
 taacgtatatt tagagagcca aggaagggtt ctgtgggggag tgggatgtaa ggtggggcct 120  
 gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca 180  
 ttccaggcag agggaacagc agtgaaa 207

<210> 150  
 <211> 111  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(111)  
 <223> n = A,T,C or G

<400> 150  
 accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg 60  
 cacttaaagt tggtcagtgt ttggacttgt taactantgg catctttggg t 111

<210> 151  
 <211> 196  
 <212> DNA  
 <213> Homo sapien

<400> 151  
 agcgcggcag gtcattatga acattccaga tacctatcat tactcgatgc tgttgataac 60  
 agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat 120  
 ggataccaac cggaaaacc cttatccgca cagcccactg tgggtcccccac tgtctacgag 180  
 gtgcattcgg ctcaagt 196

<210> 152  
 <211> 132  
 <212> DNA

<213> Homo sapien

<400> 152

acagcacttt cacatgtaag aaggagagaaa ttcctaaatg taggagaaag ataacagaac	60
cttccccctt tcatctagt gtggaaacct gatgctttat gttgacagga atagaaccag	120
gagggagttt gt	132

<210> 153

<211> 285

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(285)

<223> n = A,T,C or G

<400> 153

acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag	60
cttctgtctt tatgtctca tctgacaact ctttaccatt tttatcctcg ctcagcagga	120
gcacatcaat aaagtccaaa gtcttggact tggccttggc ttggaggag tcatcaacac	180
cctggctagt gaggggtgcg cgcgcgtcct ggatgacggc atctgtgaag tcgtgcacca	240
gtctgcaggc cctgtggaag cgcgcgtccac acggagtnag gaatt	285

<210> 154

<211> 333

<212> DNA

<213> Homo sapien

<400> 154

accacagtcc tgttgggcca gggcttcatg accctttctg tgaaaagcca tattatcacc	60
accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac	120
cctaagccgg ttacacagct aactcccact ggccttgatt tgtgaaattg ctgctgcctg	180
attggcacag gagtgcgaagg tgttcagctc ccctcctcgg tggaacgaga ctctgatttg	240
agtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat cgggagaatg	300
gtcaggcctg tctcatccat atggatcttc cgg	333

<210> 155

<211> 308

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(308)

<223> n = A,T,C or G

<400> 155

actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg	60
gaaagtgtct tgggaactgt aaagtgccta acacatgac gatgattttt gttataatat	120
ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag cccagcccc	180
atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt cttcttggt	240
gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcattgctg	300
gccctggt	308

<210> 156

<211> 295

<212> DNA



tgtaaatect	gccagtcctt	ctcttcaagc	caggggtgcat	cctcagaaac	ctactcaaca	300
cagcactcta	ggcagccact	atcaatcaat	tgaagttgac	actctgcatt	aratctattt	360
gccatttcaa	aaaaaaaaaa	aaaa				384

&lt;210&gt; 184

&lt;211&gt; 496

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(496)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 184

accgaattgg	gaccgctggc	ttataagcga	tcatgtyynt	ccrgtatcac	ctcaacgagc	60
agggagatcg	agtcctatacg	ctgaagaaat	ttgacccgat	gggacaacag	acctgctcag	120
cccatcctgc	tcggttctcc	ccagatgaca	aatactctsg	acaccgaatc	accatcaaga	180
aacgcttcaa	ggtgctcatg	acccagcaac	cgcgccctgt	cctctgaggg	tcccttaaac	240
tgatgtcttt	tctgccacct	gttacccttc	ggagactccg	taaccaaact	cttcggactg	300
tgagccctga	tgcttttttg	ccagccatac	tctttggcat	ccagtctctc	gtggcgattg	360
attatgcttg	tgtgaggcaa	tcatgggtgg	atcaccata	aagggaacac	atttgacttt	420
tttttctcat	attttaaatt	actacmagaw	tattwmagaw	waaatgawtt	gaaaaactst	480
taaaaaaaaa	aaaaaa					496

&lt;210&gt; 185

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 185

gctggtagcc	tatggcgkcg	cccacggagg	ggctcctgag	gccacggrac	agtgacttcc	60
caagtatcyt	gcgcsgcgtc	ttctaccgtc	cctacctgca	gatcttcggg	cagattcccc	120
aggaggacat	ggacgtggcc	ctcatggagc	acagcaactg	ytctctggag	cccggcttct	180
gggcacaccc	tcttggggcc	caggcgggca	cctgcgtctc	ccagtatgcc	aactggctgg	240
tggtgctgct	cctcgtcac	ttcctgctcg	tggccaacat	cctgctgggt	aacttgctca	300
ttgccatgtt	cagttacaca	ttcggcaaag	tacagggcaa	cagcgatctc	tactgggaag	360
gcgcagcgtt	accgcctcat	ccgg				384

&lt;210&gt; 186

&lt;211&gt; 577

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(577)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 186

gagttagctc	ctccacaacc	ttgatgaggt	cgtctgcagt	ggcctctcgc	ttcataccgc	60
tnccatcgtc	atactgtagg	tttgccacca	cytcctggca	tcttggggcg	gcntaatatt	120
ccaggaaact	ctcaatcaag	tcaccgtcga	tgaaacctgt	gggctgggtc	tgtcttcgcg	180
tcggtgtgaa	aggatctccc	agaaggagtg	ctcgatcttc	cccacacttt	tgatgacttt	240
attgagtcga	ttctgcatgt	ccagcaggag	gttggtaccag	ctctctgaca	gtgaggtcac	300
cagccctatc	atgccgttga	mcgtgccgaa	garcaccgag	ccttggtgtg	gggkkgaggt	360
ctcaccacga	ttctgcatta	ccagagagcc	gtggcaaaa	acattgacaa	actcgccag	420
gtggaaaaag	amcamctcct	ggargtgctn	gccgctcctc	gtcmgttggt	ggcagcgctw	480

<213> Homo sapien

<400> 156

accttgctcg	gtgcttgga	catattagga	actcaaaata	tgagatgata	acagtgccta	60
ttattgatta	ctgagagAAC	tgtagacat	ttagttgaag	attttctaca	caggaactga	120
gaataggaga	ttatgtttgg	ccctcatatt	ctctcctatc	ctccttgccct	cattctatgt	180
ctaatatatt	ctcaatcaaa	taaggtttagc	ataatcagga	aatcgaccaa	ataccaatat	240
aaaaccagat	gtctatcctt	aagatttttca	aatagaaaac	aaattaacag	actat	295

<210> 157

<211> 126

<212> DNA

<213> Homo sapien

<400> 157

acaagtttaa	atagtgctgt	cactgtgcat	gtgctgaaat	gtgaaatcca	ccacatttct	60
gaagagcaaa	acaaattctg	tcatgtaatc	tctatcttgg	gtcgtgggta	tatctgtccc	120
cttagt						126

<210> 158

<211> 442

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(442)

<223> n = A,T,C or G

<400> 158

accactgggt	cttggaaca	cccatcctta	atagcatgat	ttttctgtcg	tgtgaaaatg	60
aanccagcag	gctgccccta	gtcagtcctt	ccttccagag	aaaaagagat	ttgagaaagt	120
gcctgggttaa	ttcaccatta	atttcctccc	ccaaactctc	tgagtcttcc	cttaatatct	180
ctgggtggttc	tgaccaaagc	aggtcatggt	ttgttgagca	tttgggatcc	cagtgaagta	240
natgtttgta	gccttgcata	cttagccctt	cccacgcaca	aacggagtgg	cagagtgggtg	300
ccaaccctgt	tttcccagtc	cacgtagaca	gattcacagt	gcggaattct	ggaagctgga	360
nacagacggg	ctctttgcag	agccgggact	ctgagangga	catgagggcc	tctgcctctg	420
tgttcattct	ctgatgtcct	gt				442

<210> 159

<211> 498

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(498)

<223> n = A,T,C or G

<400> 159

acttccaggt	aacgttggtg	tttccgttga	gcctgaactg	atgggtgacg	ttgtaggttc	60
tccaacaaga	actgaggttg	cagagcgggt	agggaaagag	gctgttccag	ttgcacctgg	120
gctgctgtgg	actgttggtg	attcctcact	acggcccaag	gttggtggaac	tggcanaaag	180
gtgtgtgtgt	gganttgagc	tcgggcggct	gtggtaggtt	gtgggctctt	caacaggggc	240
tgctgtgggt	ccggggangt	aangtggtgt	gtcacttgag	cttggccagc	tctggaaagt	300
antanattct	tctgaaggc	cagcgcttgt	ggagctggca	ngggtcantg	ttgtgtgtaa	360
cgaaccagtg	ctgctgtggg	tgggtgtana	tcctccacaa	agcctgaagt	tatgggtgtcn	420
tcaggtaana	atgtgggttc	agtgtccctg	ggcngctgtg	gaaggttgta	nattgtcacc	480

aagggaataa gctgtggt 498

<210> 160  
<211> 380  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(380)  
<223> n = A,T,C or G

<400> 160  
acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac 60  
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct 120  
ggagcatggc atagaggaag ctganaaatg tggggctctga ggaagccatt tgagtctggc 180  
cactagacat ctcatcagcc acttgtgtga agagatgcc catgaccca gatgcctctc 240  
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg 300  
gagaaaaatg gcagtttgac cgaacctggt cacaacggta gaggctgatt tctaacgaaa 360  
cttgtagaat gaagcctgga 380

<210> 161  
<211> 114  
<212> DNA  
<213> Homo sapien

<400> 161  
actccacatc cctctgagc aggcggttgt cgttcaagggt gtatttggcc ttgcctgtca 60  
cactgtccac tggccctta tccacttggt gcttaatccc tcgaaagagc atgt 114

<210> 162  
<211> 177  
<212> DNA  
<213> Homo sapien

<400> 162  
actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa 60  
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt 120  
tggtgatata taacttggca ataaccagct ctggtgatac ataaaactac tcactgt 177

<210> 163  
<211> 137  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(137)  
<223> n = A,T,C or G

<400> 163  
catttatata gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac 60  
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt 120  
catcagcggc atgatgt 137

<210> 164  
<211> 469  
<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(469)

<223> n = A,T,C or G

<400> 164

cttatcacia	tgaatgttct	cctgggcagc	gttgtgatct	ttgccacctt	cgtgacttta	60
tgcaatgcat	catgctatct	cataccta	gaggaggttc	caggagattc	aaccaggaaa	120
tgcatggatc	tcaaaggaaa	caaacaccca	ataaactcgg	agtggcagac	tgacaactgt	180
gagacatgca	cttgctacga	aacagaaatt	tcatgttgca	cccttgtttc	tacacctgtg	240
ggttatgaca	aagacaactg	ccaaagaatc	ttcaagaagg	aggactgcaa	gtatatcgtg	300
gtggagaaga	aggacccaaa	aaagacctgt	tctgtcagtg	aatggataat	ctaattgtgct	360
tctagtaggc	acagggctcc	caggccaggc	ctcattctcc	tctggcctct	aatagtcaat	420
gattgtgtag	ccatgcctat	cagtaaaaag	atntttgagc	aaacactttt		469

<210> 165

<211> 195

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(195)

<223> n = A,T,C or G

<400> 165

acagtttttt	atanatatcg	acattgccgg	cacttggtgtt	cagtttcata	aagctgggtg	60
atccgctgtc	atccactatt	ccttggttag	agtaaaaatt	attcttatag	cccatgtccc	120
tgcaggccgc	ccgcccgtag	ttctcgttcc	agtcgtcttg	gcacacaggg	tgccaggact	180
tcctctgaga	tgagt					195

<210> 166

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 166

acatcttagt	agtgtggcac	atcagggggc	catcagggtc	acagtcactc	atagcctcgc	60
cgaggtcgga	gtccacacca	ccggtgtagg	tgtgctcaat	cttgggcttg	gcgcccacct	120
ttggagaagg	gatatgctgc	acacacatgt	ccacaaagcc	tgtgaactcg	ccaaagaatt	180
tttgacagac	agcctgagca	aggggcggat	gttcagcttc	agctcctcct	tcgtcagggtg	240
gatgccaacc	tcgtctangg	tccgtgggaa	gctggtgtcc	acntcaccta	caacctgggc	300
gangatctta	taaagaggct	ccnagataaa	ctccacgaaa	cttctctggg	agctgctagt	360
nggggccttt	ttggtgaact	ttc				383

<210> 167

<211> 247

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(247)  
 <223> n = A,T,C or G

<400> 167  
 acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat 60  
 tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc 120  
 tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac 180  
 tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac 240  
 tgangtc 247

<210> 168  
 <211> 273  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(273)  
 <223> n = A,T,C or G

<400> 168  
 acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa 60  
 aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatgtt tccacaaaagg 120  
 gctgacacct gagcctgnat tttactcat ccctgagaag ccctttccag taggggtggc 180  
 aattcccaac ttcttgcca caagcttccc aggctttctc ccctggaaaa ctccagcttg 240  
 agtcccgat acactcatgg gctgccctgg gca 273

<210> 169  
 <211> 431  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(431)  
 <223> n = A,T,C or G

<400> 169  
 acagccttgg cttccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60  
 agctcagacc aggggtcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta 120  
 ctactgtcaa atgaccccc atacttcctc aaaggctgtg gtaagttttg cacaggtgag 180  
 ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacactgac 240  
 cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcactgctgg gcaccagctc 300  
 acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactgg 360  
 aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc 420  
 tcgaacactg a 431

<210> 170  
 <211> 266  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(266)  
 <223> n = A,T,C or G

```

<400> 170
acctgtgggc tgggctgtta tgcctgtgcc ggctgctgaa agggagtcca gaggtggagc      60
tcaaggagct ctgcaggcat ttgccaanc ctctccanag canagggagc aacctacact      120
ccccgctaga aagacaccag attggagtcc tgggaggggg agttgggggtg ggcatttgat      180
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct      240
tcaaagctag gggctctggca ggtgga                                     266

```

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<210> 171
<211> 1248
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(1248)
<223> n = A,T,C or G

```

```

<400> 171
ggcagccaaa tcataaacgg cgaggactgc agcccgcaact cgcagccctg gcaggcggca      60
ctgggtcatgg aaaacgaatt gttctgctcg ggctgctgg tgcattccga gtgggtgctg      120
tcagccgcac actgtttcca gaagtgaagt cagagctcct acaccatcgg gctgggcctg      180
cacagtcttg aggccgacca agagccaggg agccagatgg tggaggccag cctctccgta      240
cggcaccag agtacaacag acccttgctc gctaaccgacc tcatgctcat caagttggac      300
gaatccgtgt ccgagtcctga caccatccgg agcatcagca ttgcttcgca gtgccctacc      360
gcggggaaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc      420
gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac      480
ccgctgtacc accccagcat gttctgcgcc ggccgagggc aagaccagaa ggactcctgc      540
aacggtgact ctgggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc      600
ggaaaagccc cgtgtggcca agttggcgtg ccaggtgtct acaccaacct ctgcaaattc      660
actgagtggg tagagaaaac cgtccaggcc agttaactct ggggactggg aacctatgaa      720
attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agccccctcct      780
ccctcaggcc caggagtcca ggcccccagc cctcctccc tcaaaccaag ggtacagatc      840
cccagccctc cctccctcag acccaggagt ccagaccccc cagccctcct tccctcagac      900
ccaggagtcc agccccctcct ccctcagacc caggagtcca gacccccag cccctcctc      960
ctcagaccca ggggtccagg cccccaaccc ctctccctc agactcagag gtccaagccc      1020
ccaaccntc attccccaga cccagaggtc caggtccag cccctntcc ctcagaccca      1080
gcggtccaat gccacctaga ctntccctgt acacagtgcc ccttgtggc acgttgacct      1140
aaccttacca gttggttttt catttttngt ccctttccc tagatccaga aataaagttt      1200
aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      1248

```

```

<210> 172
<211> 159
<212> PRT
<213> Homo sapien

```

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<220>
<221> VARIANT
<222> (1)...(159)
<223> Xaa = Any Amino Acid

```

```

<400> 172
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
 1             5             10             15
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
          20             25             30
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
          35             40             45
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly

```

50	55	60
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu		
65	70	75
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe		80
	85	90
Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser		95
	100	105
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe		110
	115	120
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn		125
	130	135
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser		140
145	150	155

<210> 173  
 <211> 1265  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1265)  
 <223> n = A,T,C or G

<400> 173

ggcagcccg	actgcagcc	ctggcaggcg	gcactgggtca	tggaaaacga	attgttctgc	60
tcgggcgtcc	tggtgcatcc	gcagtgggtg	ctgtcagccg	cacactgttt	ccagaactcc	120
tacaccatcg	ggctgggect	gcacagtctt	gaggccgacc	aagagccagg	gagccagatg	180
gtggaggcca	gcctctccgt	acggcaccca	gagtacaaca	gacccttgct	cgctaacgac	240
ctcatgctca	tcaagttgga	cgaatccgtg	tccgagtctg	acaccatccg	gagcatcagc	300
attgcttcgc	agtgccctac	cgcgggggaa	tcttgccctg	tttctggctg	gggtctgctg	360
gcgaacgggtg	agctcacggg	tgtgtgtctg	ccctcttcaa	ggaggtcctc	tgcccagtcg	420
cgggggctga	cccagagctc	tgcgtcccg	gcagaatgcc	taccgtgctg	cagtgcgtga	480
acgtgtcggg	ggtgtctgag	gaggtctgca	gtaagctcta	tgaccgctg	taccaccca	540
gcatgttctg	cgccggcgga	gggcaagacc	agaaggactc	ctgcaacggg	gactctgggg	600
ggccccctgat	ctgcaacggg	tacttgccag	gccttggtgc	tttcggaaaa	gccccgtgtg	660
gccaaagtgg	cgtgccaggt	gtctacacca	acctctgcaa	attcactgag	tggaatagaga	720
aaaccgtcca	ggccagttaa	ctctggggac	tgggaaccca	tgaaattgac	ccccaaatac	780
atcctgcgga	aggaattcag	gaatatctgt	tcccagcccc	tcctccctca	ggcccaggag	840
tccaggcccc	cagccccctc	tccctcaaac	caagggtaca	gateccccagc	ccctcctccc	900
tcagaccag	gagtcagac	ccccagccc	ctcctccctc	agaccagga	gtccagcccc	960
tcctcctca	gacccaggag	tccagacccc	ccagccccctc	ctccctcaga	cccaggggtt	1020
gaggccccca	acccctcctc	cttcagagtc	agaggtccaa	gcccccaacc	cctcgttccc	1080
cagaccaga	ggtnnaggtc	ccagccccctc	ttccntcaga	cccagnggtc	caatgccacc	1140
tagattttcc	ctgnacacag	tgcccccttg	tggnangttg	acccaacctt	accagttggg	1200
ttttcatttt	tngtcccttt	cccctagatc	cagaaataaa	gtttaagaga	ngngcaaaaa	1260
aaaaa						1265

<210> 174  
 <211> 1459  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1459)  
 <223> n = A,T,C or G

&lt;400&gt; 174

ggtcagccgc	acactgtttc	cagaagtgag	tgcagagctc	ctacaccatc	gggctggggc	60
tgcacagtct	tgaggccgac	caagagccag	ggagccagat	ggtaggaggc	agcctctccg	120
tacggcacc	agagtacaac	agacccttgc	tcgctaacga	cctcatgctc	atcaagttgg	180
acgaatccgt	gtccgagtct	gacaccatcc	ggagcatcag	cattgcttcg	cagtgcctta	240
ccgcggggaa	ctcttgccct	gtttctggct	ggggtctgct	ggcgaacggt	gagctcacgg	300
gtgtgtgtct	gccctcttca	aggaggtcct	ctgccagctc	gcgggggctg	accagagct	360
ctgcgtccca	ggcagaatgc	ctaccgtgct	gcagtgcgtg	aacgtgtcgg	tgggtgtctga	420
ngaggtctgc	antaagctct	atgaccgct	gtaccacccc	ancatgttct	gcgccggcgg	480
agggcaagac	cagaaggact	cctgcaacgt	gagagagggg	aaaggggagg	gcaggcgact	540
caggggaagg	tggagaagg	ggagacagag	acacacagg	ccgcatggcg	agatgcagag	600
atggagagac	acacagggag	acagtgacaa	ctagagagag	aaactgagag	aaacagagaa	660
ataaacacag	gaataaagag	aagcaaagga	agagagaaac	agaaacagac	atggggaggc	720
agaaacacac	acacatagaa	atgcagttga	ccttccaaca	gcagggggcc	tgagggcggt	780
gacctccacc	caatagaaaa	tcctcttata	acttttgact	ccccaaaaac	ctgactagaa	840
atagcctact	gttgacgggg	agccttacca	ataacataaa	tagtcgattt	atgcatacgt	900
tttatgcatt	cagatataac	cttgttgga	attttttgat	atttctaagc	tacacagttc	960
gtctgtgaat	ttttttaaat	tgttgcaact	ctcctaaaat	ttttctgatg	tgtttattga	1020
aaaaatccaa	gtataagtgg	acttgtgcat	tcaaaccagg	gttgttcaag	gggtcaactgt	1080
gtaccagag	ggaacagtg	acacagattc	atagagtgga	aacacgaaga	gaaacaggaa	1140
aatcaagac	tctacaaaga	ggctggggcag	ggtaggtcat	gcctgtaatc	ccagcacttt	1200
gggaggcgag	gcaggcgagat	cacttgagggt	aaggagtcca	agaccagcct	ggccaaaatg	1260
gtgaaatcct	gtctgtacta	aaaatacaaa	agttagctgg	atatggtggc	aggcgccgtg	1320
aatcccagct	acttgggagg	ctgaggcagg	agaattgctt	gaatatggga	ggcagagggt	1380
gaagtgagtt	gagatcacac	cactatactc	cagctggggc	aacagagtaa	gactctgtct	1440
caaaaaaaaa	aaaaaaaaa					1459

&lt;210&gt; 175

&lt;211&gt; 1167

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1167)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 175

gcgcagccct	ggcaggcggc	actggtcatg	gaaaacgaat	tgttctgctc	gggctgctctg	60
gtgcatccgc	agtgggtgct	gtcagccgca	cactgtttcc	agaactccta	caccatcggg	120
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggg	ggaggccagc	180
ctctccgtac	ggcaccacaga	gtacaacaga	ctcttgctcg	ctaacgacct	catgtctatc	240
aagttggacg	aatccgtgtc	cgagtctgac	accatccgga	gcatacagat	tgcttcgcag	300
tgccctaccg	cggggaactc	ttgcctcgtn	tctggctggg	gtctgctggc	gaacggcaga	360
atgcctaccg	tgctgcactg	cgtgaacgtg	tccgtgggtg	ctgaggangt	ctgcagtaag	420
ctctatgacc	cgctgtacca	ccccagcatg	ttctgcgcgc	gcggagggca	agaccagaag	480
gactcctgca	acggtgactc	tggggggccc	ctgatctgca	acgggtactt	gcagggcctt	540
gtgtctttcg	gaaaagcccc	gtgtggccaa	cttggcgtgc	caggtgtcta	caccaacctc	600
tgcaaattca	ctgagtggat	agagaaaacc	gtccagncca	gttaactctg	gggactggga	660
acccatgaaa	ttgaccccc	aatacatcct	gcggaangaa	ttcaggaata	tctgttccca	720
gccccctctc	cctcaggccc	aggagtccag	gccccagcc	cctcctccct	caaaccaagg	780
gtacagatcc	ccagcccctc	ctcccctaga	cccaggagtc	cagaccccc	agccccctnt	840
ccntcagacc	caggagtcca	gccccctctc	cntcagacgc	aggagtccag	acccccccagc	900
ccntctccg	tcagaccag	gggtgcaggc	ccccaaaccc	tcntccntca	gagtcagagg	960
tccaagcccc	caacccctcg	ttccccagac	ccagaggtn	aggtcccagc	ccctcctccc	1020
tcagaccag	cgggtccaatg	ccacctagan	tntcctgtga	cacagtggcc	ccttggtggca	1080
ngttgaccca	accttaccag	ttgggttttct	attttttgtc	cctttccct	agatccagaa	1140
ataaagtnta	agagaagcgc	aaaaaaa				1167



<210> 176  
 <211> 205  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(205)  
 <223> Xaa = Any Amino Acid

<400> 176  
 Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp  
 1 5 10 15  
 Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu  
 20 25 30  
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val  
 35 40 45  
 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu  
 50 55 60  
 Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser  
 65 70 75 80  
 Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly  
 85 90 95  
 Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met  
 100 105 110  
 Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val  
 115 120 125  
 Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala  
 130 135 140  
 Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly  
 145 150 155 160  
 Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys  
 165 170 175  
 Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys  
 180 185 190  
 Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser  
 195 200 205

<210> 177  
 <211> 1119  
 <212> DNA  
 <213> Homo sapien

<400> 177  
 gcgcactcgc agccctggca ggcggcactg gtcattggaaa acgaattgtt ctgctcgggc 60  
 gtccctggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctccacacc 120  
 atcgggctgg gctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag 180  
 gccagcctct ccgtacggca cccagagtag aacagaccct tgctcgctaa cgacctcatg 240  
 ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300  
 tcgcagtgcc ctaccgctgg gaactcttgc ctggtttctg gctggggtct gctggcgaa 360  
 gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc 420  
 caaccctggc aggggtgtac catttcggca acttccagtg caaggacgtc ctgctgcac 480  
 ctactgggt gctcactact gctcactgca tcaccggaa cactgtgatc aactagccag 540  
 caccatagtt tccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600  
 actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660  
 cagttatcct cactgaattg agatttcctg cttcagtgtc agccattccc acataatttc 720  
 tgacctacag aggtgaggga tcatatagct cttcaaggat gctggtactc cctcacaaa 780

```

ttcattttctc ctgttgtagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca      840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg      900
ctcagtaacac cagggcaggt ctagcatctc ttcatttagt gtatgctgtc cattcatgca      960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg     1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc     1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaaa     1119

```

&lt;210&gt; 178

&lt;211&gt; 164

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(164)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 178

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1          5          10          15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
 20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
 35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
 50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
 65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
 85          90          95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
100          105          110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
115          120          125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
130          135          140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Thr Ala Ser
145          150          155          160
Pro Gly Thr Leu

```

&lt;210&gt; 179

&lt;211&gt; 250

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 179

```

ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct      60
ccagctgccc ccggccgggg gatgagaggg tcggagcacc cttgcccggc tgtgattgct     120
gccaggcact gttcatctca gcttttctgt ccctttgtct ccggcaagcg cttctgctga     180
aagttcatat ctggagcctg atgtcttaac gaataaaggc cccatgctcc acccgaaaaa     240
aaaaaaaaaa                                     250

```

&lt;210&gt; 180

&lt;211&gt; 202

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

```

<400> 180
actagtccag tgtggtggaa ttccattgtg ttggggcccaa cacaatggct acctttaaca      60
tcacccagac cccgcccctg cccgtgcccc acgtgctgc taacgacagt atgatgctta      120
ctctgtctact cggaaactat ttttatgtaa ttaatgtatg ctttcttgtt tataaatgcc      180
tgattttaaaa aaaaaaaaaa aa                                202

```

```

<210> 181
<211> 558
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(558)
<223> n = A,T,C or G

```

```

<400> 181
tccytthtkt naggthtthkg agacamccck agacctwaan ctgtgtcaca gacttcyngg      60
aatgthtagg cagtgttagt aatttcytcg taatgattct gttattactt tcctnattct      120
ttattctctt ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa      180
ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca      240
aaattatgca agttagtaat tactcagggg taactaaatt actttaatat gctgttgaaac      300
ctactctgtt ccttggttag aaaaaattat aaacaggact ttgttagttt gggaagccaa      360
attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw      420
ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt      480
aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc      540
caaaaaaaaa aaaaaaaaaa                                558

```

```

<210> 182
<211> 479
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(479)
<223> n = A,T,C or G

```

```

<400> 182
acagggwttk grggatgcta agsccccrga rwtggtttga tccaaccctg gcttwttttc      60
agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmg gcacccctgg      120
cstcacacag astcccgagt agctgggact acaggcacac agtcactgaa gcagggccctg      180
ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca      240
ctaagggtta actttccac ccagaaaagg caacttagat aaaatcctag agtactttca      300
tactmttcta agtcctcttc cagcctcact kkgagtcctm cytggggggtt gataggaant      360
ntctcttggc tttctcaata aartctctat ycatctcatg ttttaatttg tacgcatara      420
awtgstgara aaattaaaat gttctggtty macttttaaa aaaaaaaaaa aaaaaaaaaa      479

```

```

<210> 183
<211> 384
<212> DNA
<213> Homo sapien

```

```

<400> 183
aggcggggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc      60
agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgggtg cttcagtgtc      120
ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tggagctggt      180
gccagcacca gtggcagctc tgggtgcctgt ggtttctctc acaagtgaga ttttagatat      240

```

```
tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcacatcc 540
aagatntcgc acagcactna tccagttggg attaaat 577
```

```
<210> 187
<211> 534
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(534)
<223> n = A,T,C or G
```

```
<400> 187
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw 60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact 120
ttaaacagtg tgtaaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggtg 180
tgccctattc acacctgtta aaaggcgct aagcattttt gattcaacat cttttttttt 240
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgtagcca attcactttc 300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag ctttygggagc 360
tgatatttga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg 420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctgttctg 480
aggatctccc agtttattta ccacttgca cagaaggcgt tttcttctc aggc 534
```

```
<210> 188
<211> 761
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(761)
<223> n = A,T,C or G
```

```
<400> 188
agaaaccagt atctctnaaa acaacctctc ataccttggtg gacctaatth ttgtgtgcgtg 60
tgtgtgtgcg cgcataattat atagacaggc acatcttttt tacttttgta aaagcttatg 120
cctcttttgg atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct 180
ttgtcttctg tgtaaatggg actagagaaa acacctatnt tatgagtcaa tctagttngt 240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg 300
ggggacaaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa 360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt 420
gcaaaaaaca tgtacngact tcccgttgag taatgccaaag ttgttttttt tatnataaaa 480
cttgcccttc attacatggt tnaaagtggg gtgggtgggc aaaatattga aatgatggaa 540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac 600
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaatata ctttgaacta 660
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac 720
gaaaataata acattgaaga aaaananaaa aaanaaaaaa a 761
```

```
<210> 189
<211> 482
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(482)
<223> n = A,T,C or G
```

<400> 189  
tttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca 60  
caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca 120  
aagccgcctg ctgcctttct tgtctgtctc ctgggtgcagg cacatgggga gaccttcccc 180  
aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag 240  
tgataggcac agggcaccgc gtacagaccc ctccggtcct gacaggtnga tttcgaccag 300  
gtcattgtgc cctgcccagg cacagcgta atctggaaaa gacagaatgc tttccttttc 360  
aaatttggct ngtcatngaa ngggcanttt tccaanttng gctnggtctt ggtacncttg 420  
gttcggccca gtcncngtc caaaaantat tcaccnnct ccnaattgct tgcnggnccc 480  
cc 482

<210> 190

<211> 471

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(471)

<223> n = A,T,C or G

<400> 190  
tttttttttt ttttaaaaca gtttttcaca acaaaattta ttagaagaat agtggttttg 60  
aaaactctcg catccagtga gaactacat acaccacatt acagctngga atgtntcca 120  
aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag 180  
cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg attaaaattt 240  
taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt 300  
tgaaaaattt catgtatgca atccaaccaa agaacttnat tggatgatcat gantnctcta 360  
ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacncngt acaaaaaanaa 420  
tctgtaattn anttcaacct ccgtacngaa aaatnttntt tatacactcc c 471

<210> 191

<211> 402

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(402)

<223> n = A,T,C or G

<400> 191  
gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct 60  
gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa 120  
attcttcacc agtcacatct tctaggacct ttttggatcc agttagtata agctcttcca 180  
cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg 240  
ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc 300  
ctttgtgcat ccatttttaa tatacttaat agggcattgk tncactaggt taaattctgc 360  
aagagtcatc tgtctgcaaa agttgcgtta gtatatctgc ca 402

<210> 192

<211> 601

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

&lt;222&gt; (1)...(601)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 192

gagctcggat	ccaataatct	ttgtctgagg	gcagcacaca	tatncagtgc	catggnaact	60
ggtctacccc	acatgggagc	agcatgccgt	agntatataa	ggtcattccc	tgagtcagac	120
atgcytyttt	gaytaccgtg	tgccaagtgc	tggtgattct	yaacacacyt	ccatccccyt	180
cttttgtgga	aaaactggca	cttktctgga	actagcarga	catcacttac	aaattcaccc	240
acgagacact	tgaaagggtg	aacaaagcga	ytcttgcat	gctttttgtc	cctccggcac	300
cagttgtcaa	tactaacccg	ctggtttgcc	tccatcacat	ttgtgatctg	tagctctgga	360
tacatctcct	gacagtactg	aagaacttct	tcttttgttt	caaaagcarg	tcttggtgcc	420
tggtggatca	ggttcccatt	tcccagtcyg	aatgttcaca	tggtcatatt	wacttcccac	480
aaaacattgc	gatttgaggc	tcagcaacag	caaatcctgt	tccggcattg	gctgcaagag	540
cctcgatgta	gccggccagc	gccaaggcag	gcgccgtgag	ccccaccagc	agcagaagca	600
g						601

&lt;210&gt; 193

&lt;211&gt; 608

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(608)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 193

atacagccca	nataccacca	cgaagatgcg	cttggtgact	gagaacctga	tgcggtcact	60
ggtcccgetg	tagccccagc	gactctccac	ctgctggaag	cggttgatgc	tgcaactcyt	120
cccaacgcag	gcagmagcgg	gscgggtcaa	tgaactccay	tcgtggcttg	gggtkgacgg	180
tkaagtgcag	gaagaggctg	accacctcgc	ggtccaccag	gatgcccagc	tggtgcgggac	240
ctgcagcgaa	actcctcgat	ggtcatgagc	gggaagcgaa	tgaggcccag	ggccttgccc	300
agaaccttcc	gcctgttctc	tggtgctcac	tgcaactgct	gccgtgaca	ctcggtctcg	360
gaccagcgga	caaacggcrt	tgaacagccg	cacctcacgg	atgccagctg	tgctgcgctc	420
caggammgsc	accagcgtgt	ccaggtcaat	gtcgggtgaag	ccctccgcgg	gtrattggcg	480
ctgcagtgtt	tttgtcgatg	ttctccaggc	acagggtggc	cagctgcggg	tcattcgaaga	540
gtcgcgcctg	cgtgagcagc	atgaaggcgt	tgctggctcg	cagttcttct	tcaggaaactc	600
cacgcaat						608

&lt;210&gt; 194

&lt;211&gt; 392

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(392)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 194

gaacggctgg	accttgccctc	gcattgtgct	tgctggcagg	gaataccttg	gcaagcagyt	60
ccagtccgag	cagccccaga	ccgctgccgc	ccgaagctaa	gcctgcctct	ggccttcccc	120
tccgcctcaa	tgcaagaacca	gtagtgggag	cactgtgttt	agagttaaga	gtgaacactg	180
tttgatttta	cttggggaatt	tcctctgtta	tatagctttt	cccaatgcta	atttccaaac	240
aacaacaaca	aaataacatg	tttgccctgtt	aagttgtata	aaagtaggtg	attctgtatt	300
taaagaaaat	attactgtta	catatactgc	ttgcaatttc	tgtatttatt	gktinctstgg	360
aaataaatat	agttatttaa	ggttgtcant	cc			392

<210> 195  
 <211> 502  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(502)  
 <223> n = A,T,C or G

<400> 195  
 ccsttkgagg ggktkaggkyc cagtttyccga gtggaagaaa caggccagga gaagtgcgtg 60  
 ccgagctgag gcagatgttc ccacagtgc cccagagacc stgggstata gtytctgacc 120  
 cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc 180  
 aagggaaaggc cccattccgg ggstgttccc cgaggaggaa gggaaagggc tctgtgtgcc 240  
 ccccasgagg aagagggccct gagtccctggg atcagacacc ccttcacgtg tatccccaca 300  
 caaatgcaag ctccaccaagg tccccctctca gtccccctcc stacaccctg amcgccact 360  
 gscscacacc caccagagc acgccacccg ccatggggar tgtgctcaag gartcgcnng 420  
 gcarcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmstt 480  
 gctnanaaaa aaaaanaaaa aa 502

<210> 196  
 <211> 665  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(665)  
 <223> n = A,T,C or G

<400> 196  
 ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60  
 cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt 120  
 wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga 180  
 actwatattat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkatc 240  
 aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt 300  
 attaateggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact 360  
 tcacttgggt attttattgt aaatgartta caaaattcct aatttaagar aatggtatgt 420  
 watattttatt tcattaattt ctttcctkgt ttacgtwaat tttgaaaaga wtgcatgatt 480  
 tcttgacaga aatcgatcct gatgctgtgg aagtagtttg acccacatcc ctatgagttt 540  
 ttcttagaat gtataaagg ttagcccat cnaacttcaa agaaaaaat gaccacatac 600  
 tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan 660  
 aagtg 665

<210> 197  
 <211> 492  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(492)  
 <223> n = A,T,C or G

<400> 197  
 tttntttttt ttttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat 60  
 atgtttattg gagcgatcca ttatcagtga aaagatatcaa gtgtttataa natttttagg 120

```

aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag      180
aattatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa      240
caaaattcta ccttgaaact tactccatcc aaatatggga ataanagtca gcagtgatac      300
attctcttct gaacttttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct      360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc      420
catttcactc ccatcacggg agtcaatgct acctggggaca cttgtatttt gttcatnctg      480
ancntggctt aa                                                              492

```

<210> 198

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (478)

<223> n = A,T,C or G

<400> 198

```

tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa      60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac      120
tgagtatatt ttgaaaagga caagtttaaa gtanacncat attgccganc atancacatt      180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat      240
natatatgtc aatcngatth aagatacaaa acagatccta tggtagatan catcntgtag      300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta      360
agcattctag tacctctact ccatgggtta gaatcgtaca cttatgttta catatgtnc      420
gggtaagaat tgtgttaagt naanttatgg agagggtccan gagaaaaatt tgatncaa      478

```

<210> 199

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (482)

<223> n = A,T,C or G

<400> 199

```

agtgacttgt cctccaacaa aacccttga tcaagtttgt ggcactgaca atcagaccta      60
tgctagttcc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca      120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga      180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta      240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga      300
aaatttacct ggangaaaag aggccttngg ctggggacca tccattgaa ccttctctta      360
anggacttta agaanaaact accacatgtn tgtngtatcc tggtgccngg ccgtttantg      420
aacntngacn ncacccttnt ggaatanant cttgaengcn tectgaactt gctcctctgc      480
ga                                                              482

```

<210> 200

<211> 270

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1) ... (270)

<223> n = A,T,C or G



```

<400> 200
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcc a gcagttggtc      60
cgactgcgac gacggcgccg gcgacagtcg cagggtgcagc gcgggcgccct ggggtcttgc      120
aaggctgagc tgacgccgca gaggtcgtgt cacgtcccac gaccttgacg cggtcgggga      180
cagccggaac agagcccggg gaangcggga ggcctcgggg agcccctcgg gaagggcggc      240
ccgagagata cgaggtgca ggtggccgcc

```

```

<210> 201
<211> 419
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (419)
<223> n = A,T,C or G

```

```

<400> 201
tttttttttt ttttggaaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca      60
gctagcaagg taacagggtta gggcatgggtt acatgttcag gtcaacttcc tttgtcgtgg      120
ttgattgggt tgtctttatg ggggcgggggt ggggtagggg aaancgaagc anaantaaca      180
tggagtgggt gcaccctccc tgtagaacct gggtacnaaa gcttggggca gttcacctgg      240
tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatatc ttttagagag      300
tccactgtnt ctggaggagg attaggggtt cttgccaana tccaancaaa atccacntga      360
aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cgggtggcca      419

```

```

<210> 202
<211> 509
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (509)
<223> n = A,T,C or G

```

```

<400> 202
tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt      60
tggcaacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng      120
gtntttttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaattnaa      180
tacnncnaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa      240
aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atnttttnaa      300
ggaactaaaa taaaaaaaaa cactnccgca aaggttaaag ggaacaacaa attcntttta      360
caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng      420
ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca      480
caatggnaat nccnccnncn tggactagt

```

```

<210> 203
<211> 583
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1) ... (583)
<223> n = A,T,C or G

```

```

<400> 203
tttttttttt ttttttttga cccccctctt ataaaaaaca agttaccatt ttatttttact    60
tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac    120
taaattgaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt    180
gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc    240
atttttcttg tctttaaaat tatctaattc ttccattttt tccctattcc aagtcaattt    300
gcttctctag cctcattttc tagctcttat ctactattag taagtggctt ttttcctaaa    360
agggaaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tattttctacc    420
tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tccttttatg    480
tccattttag tcactaaacg atatcnaaag tgccagaatg caaaagggtt gtgaacattt    540
attcaaaagc taatataaga tatttcacat actcatcttt ctg                    583

```

```

<210> 204
<211> 589
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(589)
<223> n = A,T,C or G

```

```

<400> 204
ttttttttnt tttttttttt ttttttnctc ttcttttttt ttganaatga ggatcgagtt    60
tttcaactct tagatagggc atgaagaaaa ctcatctttc cagctttaaa ataacaatca    120
aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc    180
tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat    240
tgagagggtt ttcttctcta ttacacata tatttccatg tgaatttgta tcaaaccctt    300
attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnag    360
cattacaaaa ctgctcaaat tgtttgtaa gnttatccat tataattagt tnggcaggag    420
ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc    480
aaaataatta aagggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat    540
ttattnagaa tgaattcaca tgttattatt ccntagccca acacaatgg                    589

```

```

<210> 205
<211> 545
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(545)
<223> n = A,T,C or G

```

```

<400> 205
ttttnttttt ttttttcagt aataatcaga acaatattta tttttatatt taaaattcat    60
agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata    120
tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat    180
ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt    240
aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat    300
atggggtgtc actggtaaac caacacattc tgaaggatac attacttagt gatagattct    360
tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt    420
aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatnng    480
aaggattaga tatgtttcct ttgccaatat taaaaaata ataatgttta ctactagtga    540
aacc                    545

```

```

<210> 206
<211> 487

```

<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(487)  
<223> n = A,T,C or G

<400> 206  
 tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt 60  
 cattttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna 120  
 caatttataa atgtaagggtg ccattattga gtanatatat tcctccaaga gtggatgtgt 180  
 cccttctccc accaactaat gaancagcaa cattagttta attttattag tagatnatac 240  
 actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag 300  
 ttggtnagaa tgcatacanca atctnacaat caacagcaag atgaagctag gcntgggctt 360  
 tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cgggtggcaag 420  
 aactcttcga accgcttctt caaaggcngc tgccacattt gtggcntctn ttgcacttgt 480  
 ttcaaaa 487

<210> 207  
<211> 332  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(332)  
<223> n = A,T,C or G

<400> 207  
 tgaattggct aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa 60  
 tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggctactact 120  
 gcatttatag gaccttcttg tggttctgct gttacntttg aantctgaca atccttgana 180  
 atctttgcat gcagaggagg taaaagggtat tggattttca cagaggaana acacagcgca 240  
 gaaatgaagg ggcagggtt actgagcttg tccactggag ggctcatggg tgggacatgg 300  
 aaaagaaggc agcctaggcc ctggggagcc ca 332

<210> 208  
<211> 524  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(524)  
<223> n = A,T,C or G

<400> 208  
 agggcggtgt gcggagggtg ttactgtttt gtctcagtaa caataaatac aaaaagactg 60  
 gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat 120  
 tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac 180  
 tccgcgtga ttcacattta gcaaccaaca atagctcatg agtcatact tgtaaatact 240  
 ttggcgagaa tacttnttga aacttgca gaataactaa gatccaagat atttcccaaa 300  
 gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca ttacaagtc 360  
 atgagccag acactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc 420  
 tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa 480  
 aaaccattac ctgatccact tccggtaatg caccaccttg gtga 524

<210> 209  
 <211> 159  
 <212> DNA  
 <213> Homo sapien

<400> 209  
 ggggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg 60  
 tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca 120  
 caaaggactc tcgacccaaa ctgcccaga ccctctcca 159

<210> 210  
 <211> 256  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(256)  
 <223> n = A,T,C or G

<400> 210  
 actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc 60  
 actgaatttc tttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta 120  
 tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat 180  
 ttgcagggtg naaatgggan ggctgggttg ttanatgaac agggacatag gaggtaggca 240  
 ccaggatgct aaatca 256

<210> 211  
 <211> 264  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(264)  
 <223> n = A,T,C or G

<400> 211  
 acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggaagg 60  
 actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt 120  
 atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga 180  
 ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga 240  
 aaaaaggag caaatgagaa gcct 264

<210> 212  
 <211> 328  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(328)  
 <223> n = A,T,C or G

<400> 212  
 acccaaaaat ccaatgctga atatttggtc tcattattcc canattcttt gattgtcaaa 60  
 ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag 120  
 gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag 180

ttnaattttca	ttcccattga	cttgggatcc	ttatcatcag	ccagagagat	tgaaaattta	240
cccctacnac	tctttactct	ctgganaggg	ccagtgggtg	tagctataag	cttggccaca	300
tttttttttc	ctttattcct	ttgtcaga				328

&lt;210&gt; 213

&lt;211&gt; 250

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(250)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 213

acttatgagc	agagcgacat	atccnagtgt	agactgaata	aaactgaatt	ctctccagtt	60
taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaaagta	agccaaggct	120
cattatgcca	aagganatat	acatttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataanc	catgttaana	aacaaatata	tctctnacct	240
tctcatcggt						250

&lt;210&gt; 214

&lt;211&gt; 444

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(444)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 214

accagaatc	caatgctgaa	tatttggtt	cattattccc	agattctttg	attgtcaaag	60
gatttaattg	tgtctcagct	tgggcacttc	agttaggacc	taaggatgcc	agccggcagg	120
tttatatatg	cagcaacaat	attcaagcgc	gacaacagggt	tattgaactt	gccccccagt	180
tgaatttcat	tcccattgac	ttgggatcct	tatcatcagc	canagagatt	gaaaatttac	240
ccctacgact	ctttactctc	tggagagggc	cagtgggtgt	agctataagc	ttggccacat	300
tttttttttc	tttattcctt	tgtcagagat	gcgattcact	catatgctan	aaaccaacag	360
agtgactttt	acaaaattcc	tataganatt	gtgaataaaa	ccttacctat	agttgccatt	420
actttgctct	ccctaataata	cctc				444

&lt;210&gt; 215

&lt;211&gt; 366

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(366)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 215

acttatgagc	agagcgacat	atccaagtgt	anactgaata	aaactgaatt	ctctccagtt	60
taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaaagta	agccaaggct	120
cattatgcca	aagganatat	acatttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataagc	catgttgaga	aacaaatata	tctctgacct	240
tctcatcggt	aagcagaggc	tgtaggcaac	atggaccata	gcgaanaaaa	aacttagtaa	300
tccaagctgt	tttctacact	gtaaccagggt	ttccaaccaa	ggtggaaatc	tcctataact	360

ggtgcc

366

<210> 216  
 <211> 260  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(260)  
 <223> n = A,T,C or G

<400> 216  
 ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc 60  
 caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc atttttttat 120  
 taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa 180  
 atcaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat 240  
 aattcttcct tccctccttt 260

<210> 217  
 <211> 262  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(262)  
 <223> n = A,T,C or G

<400> 217  
 acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta 60  
 tcttgccctat aattttctat tttaataagg aaatagcaaaa ttgggggtggg gggaatgtag 120  
 ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt 180  
 atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta 240  
 atatecttca tgcttgtaaa gt 262

<210> 218  
 <211> 205  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(205)  
 <223> n = A,T,C or G

<400> 218  
 accaaggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca 60  
 cccctatcaa ctcccttttg tagtaaaactt ggaaccttgg aaatgaccag gccaagactc 120  
 aggctcccc agttctactg acctttgtcc ttangtntna ngtccagggt tgctaggaaa 180  
 anaaatcagc agacacaggt gtaaa 205

<210> 219  
 <211> 114  
 <212> DNA  
 <213> Homo sapien

<400> 219

tactgttttg tctcagtaac aataaatata aaaagactgg ttgtgttccg gccccatcca 60  
accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220  
<211> 93  
<212> DNA  
<213> Homo sapien

<400> 220  
actagccagc acaaaaggca gggtagcctg aattgctttc tgctctttac atttctttta 60  
aaataagcat ttagtgctca gtccctactg agt 93

<210> 221  
<211> 167  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(167)  
<223> n = A,T,C or G

<400> 221  
actangtgca ggtgcgacaca aatatttgct gatattccct tcattcttga ttccatgagg 60  
tcttttgccc agcctgtggc tctactgtag taagtctctg ctgatgagga gccagnatgc 120  
ccccactac cttccctgac gctccccana aatcacccaa cctctgt 167

<210> 222  
<211> 351  
<212> DNA  
<213> Homo sapien

<400> 222  
agggcgtggt gcggagggcg gtactgacct cattagtagg aggatgcatt ctggcacccc 60  
gttcttcacc tgtcccccaa tccttaaaaag gccatactgc ataaagtcaa caacagataa 120  
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180  
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240  
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt 300  
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t 351

<210> 223  
<211> 383  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(383)  
<223> n = A,T,C or G

<400> 223  
aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60  
tggttaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga 120  
ttaaagtgtc tgtgccaaaa ttttgatttt tatttgagga cttcttatca aaagtaatgc 180  
tgccaaagga agtctaagga attagtagtg tccccmtcac ttgtttggag tgtgctatc 240  
taaaagattt tgatttcctg gaatgacaat tatattttta ctttgggtggg ggaaanagtt 300  
ataggaccac agtcttcact tctgatactt gtaaatattt cttttattgc acttgttttg 360  
accattaagc tatatgttta aaa 383

<210> 224  
 <211> 320  
 <212> DNA  
 <213> Homo sapien

<400> 224  
 cccctgaagg cttcttggtta gaaaatagta cagttacaac caataggaac aacaaaaaga 60  
 aaaagtttgt gacattgttag tagggagtgt gtacccctta ctcccatca aaaaaaaat 120  
 ggatacatgg ttaaaggata raagggaat atttatcat atgttctaaa agagaaggaa 180  
 gagaaaatac tactttctcr aaatggaagc ccttaaagggt gctttgatac tgaaggacac 240  
 aaatgtggcc gtccatcctc ctttaragtt gcatgacttg gacacggtaa ctggtgcagt 300  
 tttaractcm gcattgtgac 320

<210> 225  
 <211> 1214  
 <212> DNA  
 <213> Homo sapien

<400> 225  
 gaggactgca gcccgcactc gcagccctgg caggcggcac tggatcatgga aaacgaattg 60  
 ttctgctcgg gcgtcctgggt gcaccccgag tgggtgctgt cageccgaca ctggttccag 120  
 aactcctaca ccatcgggct gggcctgcac agtcttgagg ccgaccaaga gccagggagc 180  
 cagatggttg aggccagcct ctccgtacgg caccagagt acaacagacc cttgctcgtc 240  
 aacgacctca tgctcatcaa gttggacgaa tccgtgtccg agtctgacac catccggagc 300  
 atcagcattg cttcgcagtg ccctaccgag gggaaactctt gcctcgtttc tggctgggggt 360  
 ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaacgtgtc ggtggtgtct 420  
 gaggaggtct gcagtaagct ctatgaccog ctgtaccacc ccagcatgtt ctgcgcgggc 480  
 ggagggcaag accagaagga ctccctgcaac ggtgactctg gggggccctt gatctgcaac 540  
 ggtgacttgc agggccttgt gtctttcgga aaagcccggt gtggccaagt tggcgtgcca 600  
 ggtgtctaca ccaacctctg caaattcact gagtggatag agaaaaccgt ccaggccagt 660  
 taactctggg gactgggaac ccatgaaatt gaccccaaa tacatcctgc ggaagggaatt 720  
 caggaatatc tgttcccagc ccctcctccc tcaggcccag gagtccaggc cccagcccc 780  
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 gacccccag ccctcctccc ctccagccca ggagtccagc ccctcctccc tcagaccag 900  
 gagtccagac cccccagccc ctccctccctc agaccagggt gtccaggccc ccaaccctc 960  
 ctccctcaga ctccagaggtc caagccccc accctcctt cccagagccc agaggtccag 1020  
 gtcccagccc ctccctccctc agaccagcg gtccaatgcc acctagactc tccctgtaca 1080  
 cagtgcctcc ttgtggcagc ttgaccacac cttaccagtt ggtttttcat tttttgtccc 1140  
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 aaaaaaaaaa aaaa 1214

<210> 226  
 <211> 119  
 <212> DNA  
 <213> Homo sapien

<400> 226  
 acccagtatg tgcagggaga cggaacccca tgtgacagcc cactccacca gggttcccaa 60  
 agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacg ataaccagt 119

<210> 227  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<400> 227  
 acaattcata gggacgacca atgaggacag ggaatgaacc cggctctccc ccagccctga 60



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acggacgggtt	cttagcacaa	tttgtgaaat	ctgtgtaraa	ccgggctttg	caggggagat	180
aattttcctc	ctctggagga	aaggtgggtga	ttgacaggca	gggagacagt	gacaaggcta	240
gagaaagcca	cgctcggcct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttgtcccc	ttccaatcag	ccactttctga	gaacccccat	ctaacttcct	actggaaaag	360
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gacaggctct	gccctcaagc	cggctgaggg	cagcaaccac	tctcctcccc	tttctcacgc	660
aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggct	720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
gtccacttct	agggttttcag	cctagatggg	agtcgtgt			818

&lt;210&gt; 228

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 228

actggagaca	ctgttgaact	tgatcaagac	ccagaccacc	ccaggtctcc	ttcgtgggat	60
gtcatgacgt	ttgacatacc	tttggaaacga	gcctcctcct	tggagatgg	aagaccgtgt	120
tcgtagccga	cctggcctct	cctggcctgt	ttcttaagat	gcggagtcac	atttcaatgg	180
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tgctcgggtc	acattggggg	gctttgggat	aaaagattta	tgagccaact	attctctggc	300
accagattct	aggccagttt	gttccactga	agcttttccc	acagcagtcc	acctctgcag	360
gctggcagct	gaatggcttg	ccggtggctc	tgtggcaaga	tcacactgag	atcgatgggt	420
gagaaggcta	ggatgcttgt	ctagtgttct	tagctgtcac	gttggctcct	tccaggttgg	480
ccagacgggtg	ttggccactc	ccttctaaaa	cacaggcgcc	ctcctgggtga	cagtgacccg	540
ccgtgggatg	ccttggccca	ttccagcagt	cccagttatg	catttcaagt	ttggggtttg	600
ttcttttctg	taattgttct	ctgtgttgtc	agctgtcttc	atttctggg	ctaagcagca	660
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cttcactctg	aagtagctgg	tggt				744

&lt;210&gt; 229

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 229

cgagtctggg	ttttgtctat	aaagtttgat	ccctcctttt	ctcatccaaa	tcatgtgaac	60
cattacacat	cgaaataaaa	gaaaggtggc	agacttgccc	aacgccaggc	tgacatgtgc	120
tgcagggttg	ttgtttttta	attattattg	ttagaaacgt	caccacacagt	ccctgttaat	180
ttgtatgtga	cagccaactc	tgagaaggtc	ctattttttc	acctgcagag	gatccagtct	240
cactaggctc	ctccttgccc	tcacactgga	gtctccgcca	gtgtgggtgc	ccactgacat	300

&lt;210&gt; 230

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 230

cagcagaaca	aatacaaaata	tgaagagtgc	aaagatctca	taaaatctat	gctgaggaat	60
gagcgacagt	tcaaggagga	gaagcttgca	gagcagctca	agcaagctga	ggagctcagg	120
caatataaag	tcctggttca	cactcaggaa	cgagagctga	cccagttaag	ggagaagtgt	180
cggaaggga	gagatgcctc	cctctcattg	aatgagcatc	tccaggccct	cctcactccg	240
gatgaaccgg	acaagtccca	ggggcaggac	ctccaagaaa	cagacctcgg	ccgcgaccac	300
g						301

<210> 231  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 231  
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 caggaactcc aagtccacat ccttggcaac tggggacttg cgcaggttag ccttgaggat 120  
 ggcaacacgg gacttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg 180  
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggta ccgccaatga tgaacacatt 240  
 tttttttgtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc 300  
 c 301

<210> 232  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 232  
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 ggcgacagcg gggcttcctg attctggaat ataactttgt gtaaattaac agccacctat 120  
 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtcctgtcca 180  
 cgtgctgtac caagtgtctg tgccagcctg ttacctgttc tcaactgaaa tctggctaatt 240  
 gctcttctgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300  
 g 301

<210> 233  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 233  
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 atgctaaggc cccagagatc gtttgatcca accctcttat tttcagaggg gaaaatgggg 120  
 cctagaagtt acagagcatc tagctggtgc gctggcacc cttggcctcac acagactccc 180  
 gagtagctgg gactacaggg acacagtcac tgaagcaggc cctgttagca attctatgcg 240  
 tacaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa 300  
 c 301

<210> 234  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 234  
 aggtcctaca catcgagact catccatgat tgatatgaat ttaaaaatta caagcaaaga 60  
 cattttattc atcatgatgc tttcttttgt ttcttctttt cgttttcttc tttttctttt 120  
 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180  
 cgcctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgcc 240  
 ttgatcacca gcttaatggt cagatcatct gcttcaatgg ctctgtcagt atagttcttc 300  
 t 301

<210> 235  
 <211> 283  
 <212> DNA  
 <213> Homo sapien

<400> 235  
 tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg 60  
 aattccctca tcttttaggg aatcattttac cagggtttgga gaggattcag acagctcagg 120  
 tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata 180  
 atgttatctt tgaactgatg ctcataggag agaataaag aactctgagt gatatcaaca 240  
 ttagggattc aaagaaatat tagatttaag ctcacactgg tca 283

<210> 236  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 236  
 aggtcctcca ccaactgcct gaagcacggg taaaattggg aagaagtata gtgcagcata 60  
 aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg 120  
 tcggagcagc atcattaata ccaagcagaa tgcgtaatag ataaatacaa tggatatatag 180  
 tgggtagacg gcttcatgag tacagtgtac tgtgggtatcg taatctggac ttggggttga 240  
 aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc 300  
 a 301

<210> 237  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 237  
 cagtggtagt ggtgggtggac gtggcggttg tctggtgtgcc ttttttggtg cccgtcacaa 60  
 actcaatttt tgttgcgtcc tttttggcct tttccaattt gtccatctca attttctggg 120  
 ccttggtcaa tgctcatag taggagtcct cagaccagcc atggggatca aacatatcct 180  
 ttgggtagtt ggtgccaagc tctcaatgg cacagaatgg atcagcttct cgtaaactca 240  
 gggttccgaa attctttctt cctttggata atgtagtcca tatccattcc ctcctttatc 300  
 t 301

<210> 238  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 238  
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 gttcacagtt cagccccctg ctcaaaaaac caacgggcca gctaaggaga ggaggaggca 120  
 ccttgagact tccggagtcg aggtctctcca gggttcccca gcccatcaat cattttctgc 180  
 accccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca 240  
 gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta 300  
 t 301

<210> 239  
 <211> 239  
 <212> DNA  
 <213> Homo sapien

<400> 239  
 ataagcagct aggggaattct ttatttagta atgtcctaac ataaaagtgc acataactgc 60  
 ttctgtcaaa ccatgatact gagctttgtg acaaccaga aataactaag agaaggcaaa 120  
 cataatacct tagagatcaa gaaacattta cacagttcaa ctgtttaaaa atagctcaac 180  
 attcagccag tgagtagagt gtgaatgcc gcatcacag tatacaggtc cttcaggga 239

<210> 240

<211> 300  
 <212> DNA  
 <213> Homo sapien

<400> 240  
 ggctcctaag aagcagcagc ttccacattt taacgcaggt ttacggtgat actgtccttt 60  
 gggatctgcc ctccagtggg acctttttaag gaagaagtgg gcccaagcta agttccacat 120  
 gctgggtgag ccagatgact tctgttccct ggctactttc ttcaatgggg cgaatggggg 180  
 ctgccagggt tttaaaatca tgcttcatct tgaagcacac ggctacttca cctcctcac 240  
 gctgtgggtg tactttgatg aaaatacca ctttgttggc ctttctgaag ctataatgtc 300

<210> 241  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 241  
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 cctcttttga ggaactcca gcagctatgt tgggtgtctt gagggaatgc aacaaggctg 120  
 ctctcccatg tattggaaaa ctgcaactg gactcaactg gaaggaagtg ctgctgccag 180  
 tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtcttttct 240  
 tctcctcct gtcatacggg ctctctcaag catcctttgt tgtcaggggc ctaaaaggga 300  
 g 301

<210> 242  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 242  
 ccgaggtcct gggatgcaac caatcactct gtttcacgtg acttttatca ccatacaatt 60  
 tgtggcattt cctcattttc tacattgtag aatcaagagt gtaaataaat gtatatcgat 120  
 gtcttcaaga atatatacatt cctttttcac tagaaccat tcaaaatata agtcaagaat 180  
 cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta 240  
 taagtaccca aagttttata aatcaaaagc cctaatagata accattttta gaattcaatc 300  
 a 301

<210> 243  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 243  
 aggtaagtcc cagtttgaag ctcaaaagat ctggtatgag cataggctca tcgacgacat 60  
 ggtggcccaa gctatgaaat cagagggagg cttcatctgg gcctgtaaaa actatgatgg 120  
 tgacgtgcag tcggactctg tggcccaagg gtatggctct ctcggcatga tgaccagcgt 180  
 gctggtttgt ccagatggca agacagtaga agcagaggct gccacggga ctgtaaccgc 240  
 tcactaccgc atgttccaga aaggacagga gacgtccacc aatcccattg cttccatttt 300  
 t 301

<210> 244  
 <211> 300  
 <212> DNA  
 <213> Homo sapien

<400> 244  
 gctggtttgc aagaatgaaa tgaatgatcc tacagctagg acttaacctt gaaatggaaa 60  
 gtcagtcaat cccatttgca ggatctgtct gtgcacatgc ctctgtagag agcagcatcc 120

ccagggacct	tggaaacagt	tgacactgta	aggtgcttgc	tccccaagac	acatcctaaa	180
aggtgttgta	atgggtgaaaa	cgtcttcctt	ctttattgcc	ccttccttatt	tatgtgaaca	240
actgtttgtc	ttttgtgtat	ctttttttaa	ctgtaaagtt	caattgtgaa	aatgaatatac	300

<210> 245  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 245						
gtctgagtat	ttaaaatggt	attgaaatta	tccccaacca	atgttagaaa	agaaagaggt	60
tatatactta	gataaaaaat	gaggtgaatt	actatccatt	gaaatcatgc	tcttagaatt	120
aaggccagga	gatattgtca	ttaatgtara	cttcaggaca	ctagagtata	gcagccctat	180
gttttcaaag	agcagagatg	caattaaata	ttgttttagca	tcaaaaaggc	cactcaatac	240
agctaataaa	atgaaagacc	taatttctaa	agcaattcct	tataatttac	aaagttttaa	300
g						301

<210> 246  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 246						
ggtctgtcct	acaatgcctg	cttcttgaaa	gaagtcggca	ctttctagaa	tagctaaata	60
acctgggctt	attttaaaga	actatttgta	gctcagattg	gttttcctat	ggctaaaata	120
agtgtcttct	gtgaaaatta	aataaaacag	ttaattcaaa	gccttgatat	atgttaccac	180
taacaatcat	actaaatata	ttttgaagta	caaagtttga	catgctctaa	agtgacaacc	240
caaatgtgtc	ttacaaaaca	cgttcctaac	aaggtatgct	ttacactacc	aatgcagaaa	300
c						301

<210> 247  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 247						
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gcctaagagg	gcgactggcg	gcagcacaac	caagggaaggc	aagggtgttt	ccccacgct	120
gtgtcctgtg	ttcaggtgcg	acacacaatc	ctcatgggaa	caggatcacc	catgcgctgc	180
ccttgatgat	caagggtggg	gcttaagtgg	attaaggagg	gcaagttctg	ggttccttgc	240
cttttcaaac	catgaagtca	ggctctgtat	ccctcctttt	cctaactgat	attctaacta	300
a						301

<210> 248  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 248						
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attaggaaga	ttcttagggg	taatttttct	gaggaaggag	aactagccaa	cttaagaatt	120
acaggaagaa	agtggttttg	aagacagcca	aagaaataaa	agcagattaa	attgtatcag	180
gtacattcca	gcctgttggc	aactccataa	aaacatttca	gatttttaatc	ccgaatttag	240
ctaattgagac	tggatttttg	ttttttatgt	tgtgtgtcgc	agagctaaaa	actcagttcc	300
c						301

<210> 249  
 <211> 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 249

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gtccagagga agcacctggt gctgaactag gcttgccctg ctgtgaactt gcacttggag      60
ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgccccgcc      120
ccagggagac acagcagtga ctcagagctg gtcgcacact gtgcctccct cctcaccgcc      180
catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag      240
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt      300
a                                                                                   301

```

&lt;210&gt; 250

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 250

```

ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacactttct      60
cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc      120
cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac      180
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta      240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc      300
a                                                                                   301

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&lt;210&gt; 251

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 251

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gccgaggtcc tacatttggc ccagtttccc cctgcaccc ctcaggggcc cctgcctcat      60
agacaacctc atagagcata ggagaactgg ttgccttggg ggcaggggga ctgtctggat      120
ggcagggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct      180
cattggggatc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccgga      240
cctctggagg ggggcagtg aatcccagct ccaggacgga tcctgtcgaa aagatatact      300
c                                                                                   301

```

&lt;210&gt; 252

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 252

```

gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgtgg catttcctca      60
ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata      120
tcatttcctt ttacttagga acccattcaa aatataagtc aagaatctta atatcaacaa      180
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag taccctaaagt      240
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc      300
a                                                                                   301

```

&lt;210&gt; 253

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 253

```

ttccctaaga agatgttatt ttgttggggt ttgttcccc tccatctcga ttctcgtacc      60
caactaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctccttagct      120

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tggtctgatt gttttcagac cttaaaatat aaacttgttt cacaagcttt aatccatgtg 180
gatttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt 240
tccatagtgc ccacagggtg ttcctcacat tttctccata ggaaaatgct ttttcccaag 300
g 301
```

<210> 254  
<211> 301  
<212> DNA  
<213> Homo sapien

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<400> 254
cgctgcgcct ttcccttggg ggaggggcaa ggccagaggg ggtccaagtg cagcacgagg 60
aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaatcccc 120
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa 180
gaaaaaata aagcttttga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc 240
acttaaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc 300
t 301
```

<210> 255  
<211> 302  
<212> DNA  
<213> Homo sapien

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<400> 255
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attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat 120
tgggattttt ttgagttctt caagcatctc ctaataccct caagggcctg agtagggggg 180
aggaaaaagg actggagggtg gaatctttat aaaaaacaag agtgattgag gcagattgta 240
aacattatta aaaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac 300
aa 302
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<210> 256  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

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<400> 256
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acccccaaaa gcctggacac cttgagcaca cagttagtac caggacagac tcatctctat 180
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt 240
gtggcctctc ggctgggtta gcaagaacat tcagggtagg cctaagttnan tcgtgttagt 300
t 301
```

<210> 257  
<211> 301  
<212> DNA  
<213> Homo sapien

```
<400> 257
gttgtggagg aactctggct tgctcattaa gtcctactga ttttactat cccctgaatt 60
tccccactta tttttgtctt tcaactatgc aggccttaga agaggtctac ctgcctccag 120
tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat 180
```





<400> 261  
aaatattcga gcaaatacctg taactaatgt gtctccataa aaggctttga actcagtga 60  
tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggt 120  
agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aagggttcaat 180  
ggtgacatcc aattttcttct gataatttag attcctcaca accttcctag ttaagtgaag 240  
ggcatgatga tcatccaaag cccagtgggc acttactcca gactttctgc aatgaagatc 300  
a 301

<210> 262  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 262  
gaggagagcc tggtacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc 60  
tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatcc ctgagtcacc 120  
cctagacttc ctaaacccaga tcctctgggg ctggaacctg gcactctgca tttgtaatga 180  
gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgcc 240  
catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300  
c 301

<210> 263  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 263  
tttagcttgt ggtaaatacgc tcacaaaact gatttttaaaa tcaagttaat gtgaattttg 60  
aaaattacta cttaataccta attcacaata acaatggcat taaggtttga cttgagttgg 120  
ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat 180  
taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg 240  
agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg 300  
g 301

<210> 264  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 264  
aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc 60  
aatgaatgac tctaaaaaca atattttacat ttaatggttt gtagacaata aaaaaacaag 120  
gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag 180  
ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240  
acccttcata taaattcact atcttggtt gaggcactcc ataaaatgta tcacgtgcat 300  
a 301

<210> 265  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 265

tgcccaagtt	atgtgtaagt	gtatccgcac	ccagaggtaa	aactacactg	tcattctttgt	60
cttcttgtga	cgcagtattt	cttctctggg	gagaagccgg	gaagtcttct	cctggctcta	120
catattcttg	gaagtctcta	atcaactttt	gttccatttg	tttcatttct	tcaggaggga	180
ttttcagttt	gtcaacatgt	tctctaacaa	cacttgccca	tttctgtaaa	gaatccaaag	240
cagttccaagg	ctttgacatg	tcaacaacca	gcataactag	agtatccttc	agagatacgg	300
c						301

<210> 266  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 266						
taccgtctgc	ccttctctcc	atccaggcca	tctgcgaatc	tacatgggtc	ctcctattcg	60
acaccagatc	actcttttct	ctaccacag	gcttgctatg	agcaagagac	acaacctctc	120
ctcttctgtg	ttccagcttc	ttttctgtt	cttcccaccc	cttaagttct	attcctgggg	180
atagagacac	caatacccat	aacctctctc	ctaagcctcc	ttataacca	gggtgcacag	240
cacagactcc	tgacaactgg	taaggccaat	gaactgggag	ctcacagctg	gctgtgcctg	300
a						301

<210> 267  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 267						
aaagagcaca	ggccagctca	gcctgccctg	gccatctaga	ctcagcctgg	ctccatgggg	60
gttctcagtg	ctgagtcct	ccaggaaaag	ctcacctaga	ccttctgagg	ctgaatcttc	120
atcctcacag	gcagcttctg	agagcctgat	attcctagcc	ttgatggtct	ggagtaaagc	180
ctcattctga	ttcctctcct	tcttttcttt	caagttggct	ttcctcacat	ccctctgttc	240
aattcgcttc	agcttgtctg	ctttagccct	catttccaga	agcttcttct	ctttggcatc	300
t						301

<210> 268  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 268						
aatgtctcac	tcaactactt	cccagcctac	cgtggcctaa	ttctgggagt	tttcttctta	60
gatcttggga	gagctgggtc	ttctaaggag	aaggaggaag	gacagatgta	actttggatc	120
tcgaagagga	agtctaattg	aagtaattag	tcaacgggtcc	ttgttttagac	tcttggaata	180
tgctgggtgg	ctcagtgagc	ccttttggag	aaagcaagta	ttattcttaa	ggagtaacca	240
cttcccatg	ttctactttc	taccatcatc	aattgtatat	tatgtattct	ttggagaact	300
a						301

<210> 269  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 269						
taacaatata	cactagctat	ctttttaact	gtccatcatt	agcaccaatg	aagattcaat	60
aaaattacct	ttattcacac	atctcaaaac	aattctgcaa	attcttagtg	aagtttaact	120
atagtcacag	accttaaata	ttcacattgt	tttctatgtc	tactgaaaat	aagttcacta	180
cttttctgga	tattctttac	aaaatcttat	taaaattcct	ggtattatca	cccccaatta	240
tacagtagca	caaccacctt	atgtagtttt	tacatgatag	ctctgtagaa	gtttcacatc	300
t						301

<210> 270  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 270  
cattgaagag cttttgcgaa acatcagaac acaagtgtt ataaaattaa ttaagcctta 60  
cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga 120  
gagcttgctg gtgcagtgc tttggataa cactattcat ggccgaattg atcaagtcaa 180  
ccaactcctt gaactggatc atcagaagaa ggggtgtgca cgatatactg cactagataa 240  
tggaaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggctt aacagaaaac 300  
a 301

<210> 271  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 271  
aaaaggttct cataagatta acaattttaa taaatatattg atagaacatt ctttctcatt 60  
tttatagctc atcttttagg ttgatattca gttcatgtt cccttgctgt tcttgatcca 120  
gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt gggtcceaagg 180  
tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240  
tctctcctcc agatganaac tgatcatgcg cccacatttt gggttttata gaagcagtca 300  
c 301

<210> 272  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 272  
taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaagtgc 60  
ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120  
tccaataatt ccctcatgat gagcaagaaa aattctttgc gcaccctcc tgcattccaca 180  
gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc 240  
ctaaggactt ccattgcac tctacaata ttttctctac gcaccactag aattaagcag 300  
g 301

<210> 273  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 273  
acatgtgtgt atgtgtatct ttgggaaaaa aanaagacat cttgtttayt atttttttgg 60  
agagangctg ggacatggat aatcacwtaa tttgtayta tyactttaat ctgactygaa 120

```

gaaccgtcta aaaataaaat ttaccatgtc dtatatctcct tatagtatgc ttatttcacc 180
ttytttctgt ccagagagag tatcagtgc ananatttma ggggtgaamac atgmattgggt 240
gggacttnty ttacngagm accctgcccg sgcgcctcg makcngantt ccgcsananc 300
t 301

```

```

<210> 274
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 274
cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg 60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa 120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttggtg gaaaagtcca 180
tctaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc 240
aattgtgctt cttttgataa gaagctttct tggtcatatc aggaaattcc aganaaagtc 300
c 301

```

```

<210> 275
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 275
tcgggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg 60
gggtgaaatt ggccaacttt ctattaactt atgttggtgcaa ttttgccacc aacagtaagc 120
tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag 180
tcaagagact cccaggcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc 240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccctat 300
a 301

```

```

<210> 276
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 276
tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat 60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat 120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc 180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt 240
aaaactattc agtatgtttc ccttgcttca tgtctgagaa ggctctcctt caatggggat 300
g 301

```

```

<210> 277
<211> 301
<212> DNA
<213> Homo sapien

```

```

gtttatttac attacagaaa aaacatcaag acaatgtata ctatttcaaa tatatccata    60
cataatcaaa tatagctgta gtacatgttt tcattggtgt agattaccac aaatgcaagg    120
caacatgtgt agatctcttg tcttattcct ttgtctataa tactgtattg tgtagtccaa    180
gctctcggtg gtccagccac tgtgaaacat gctcccttta gattaacctc gtggacgctc    240
ttgttgtatt gctgaactgt agtgccctgt attttgcttc tgtctgtgaa ttctgttgct    300
tctggggcat ttccttgtga tgcagaggac caccacacag atgacagcaa tctgaatt    358

```

```

<210> 315
<211> 341
<212> DNA
<213> Homo sapien

```

```

<400> 315
taccacctcc ccgctggcac tgatgagccg catcaccatg gtcaccagca ccatgaaggc    60
ataggtgatg atgaggacat ggaatgggcc cccaaggatg gtctgtccaa agaagcgagt    120
gacccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac    180
agtaccagc tccccgacca gccggatatc gtccttaggg gtcatgtagg ctccctgaag    240
tagcttctgc tgtaagaggg tgttgtcccc ggggctcgtg cggttattgg tcctgggctt    300
gagggggcgg tagatgcagc acatggtgaa gcagatgatg t                    341

```

```

<210> 316
<211> 151
<212> DNA
<213> Homo sapien

```

```

<400> 316
agactgggca agactcttac gccccacact gcaatttggc cttgttgccg tatccattta    60
tgtgggcctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact    120
cattcaggga gctctggttg caatattagt t                    151

```

```

<210> 317
<211> 151
<212> DNA
<213> Homo sapien

```

```

<400> 317
agaactagtg gatcctaata aaataacctg aacatatatt ggcatttatc aatggctcaa    60
atcttcattt atctctggcc ttaacctggg ctccctgaggc tgcggccagc agatcccagg    120
ccagggtctt gttcttgcca cacctgcttg a                    151

```

```

<210> 318
<211> 151
<212> DNA
<213> Homo sapien

```

```

<400> 318
actggtggga ggcgctgttt agttggctgt tttcagaggg gtctttcgga gggacctcct    60
gctgcaggct ggagtgtctt tattcctggc gggagaccgc acattccact gctgaggctg    120
tgggggcggt ttatcaggca gtgataaaca t                    151

```

```

<210> 319
<211> 151
<212> DNA
<213> Homo sapien

```

```

<400> 319
aactagtggg tccagagcta taggtacagt gtgatctcag ctttgcaaac acattttcta    60
catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg    120

```

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 277  
 tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag 60  
 atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg 120  
 gaatcatggc actcctgata ctttcccaa tcaacactct caatgcccc cctcgtcct 180  
 caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240  
 gttcnctgtc gattacatct gaccagtctc ctttttccga agtcntccg ttcaatcttg 300  
 c 301

<210> 278  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 278  
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60  
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca 120  
 cagtctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc 180  
 aatgaacatc tcatgtgtgc tcacaatggt ctggcactat tataagtgtc tcacaggttt 240  
 tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300  
 c 301

<210> 279  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 279  
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60  
 gttatatata ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc 120  
 ttagaccttt accttccagc caccacacag tgcttgatat ttcagagtca gtcattgggtt 180  
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240  
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300  
 a 301

<210> 280  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 280  
 ggtactggag ttttcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg 60  
 tagaaagggtg gtggaaccaa attgtgggtca atggaaatag gagaatatgg ttctcactct 120

tgagaaaaaa	acctaagatt	agcccaggta	gttgctgtga	acttcagttt	ttctgcctgg	180
gtttgatata	gtttagggtt	ggggtagat	taagatctaa	attacatcag	gacaaagaga	240
cagactatta	actccacagt	taattaagga	ggtaggttcc	atgtttattt	gttaaagcag	300
t						301

&lt;210&gt; 281

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 281

aggtacaaga	aggggaatgg	gaaagagctg	ctgctgtggc	attgttcaac	ttggatattc	60
gccgagcaat	ccaaatcctg	aatgaagggg	catcttctga	aaaaggagat	ctgaatctca	120
atgtggtagc	aatggcttta	tcgggttata	cggatgagaa	gaactccctt	tgagagagaaa	180
tgtgtagcac	actgcgatta	cagctaaata	acccgtattt	gtgtgtcatg	tttgcatttc	240
tgacaagtga	aacaggatct	tacgatggag	ttttgtatga	aaacaaagt	gcagtacctc	300
g						301

&lt;210&gt; 282

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 282

caggtactac	agaattaaaa	tactgacaag	caagtagttt	cttggcgtgc	acgaattgca	60
tccagaacct	aaaaattaag	aaattcaaaa	agacattttg	tgggcacctg	ctagcacaga	120
agcgcagaag	caaagcccag	gcagaacct	gctaacctta	cagctcagcc	tgacagaag	180
cgcagaagca	aagcccaggc	agaacctatg	taaccttaca	gctcagcctg	cacagaagcg	240
cagaagcaaa	gccccaggcg	aacatgctaa	ccttacagct	cagcctgcac	agaagcacag	300
a						301

&lt;210&gt; 283

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 283

atctgtatac	ggcagacaaa	ctttatarag	tgtagagagg	tgagcgaaag	gatgcaaaag	60
cactttgagg	gctttataat	aatatgctgc	ttgaaaaaaa	aaatgtgtag	ttgatactca	120
gtgcatctcc	agacatagta	aggggttgct	ctgaccaatc	aggtgatcat	tttttctatc	180
acttcccagg	ttttatgcaa	aaattttggt	aaattctata	atggtgatat	gcattcttta	240
ggaaacatat	acatttttta	aaatctatct	tatgtaagaa	ctgacagacg	aatttgcttt	300
g						301

&lt;210&gt; 284

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 284

caggtacaaa	acgctattaa	gtggcttaga	atttgaacat	ttgtggtctt	tatttacttt	60
gcttcgtgtg	tgggcaaagc	aacatcttcc	ctaaatatat	attaccaaga	aaagcaagaa	120
gcagattagg	tttttgacaa	aacaaacagg	ccaaaagggg	gctgacctgg	agcagagcat	180
ggtgagaggc	aaggcatgag	agggcaagtt	tggtgtggac	agatctgtgc	ctactttatt	240
actggagtaa	aagaaaacaa	agttcattga	tgctgaagga	tatatacagt	gttagaaatt	300
a						301

&lt;210&gt; 285

<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 285  
acatcaccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc 60  
aatgatcatt agtgttttaa aaaaaaatact gaaaactcct tctgcatccc aatctctaac 120  
caggaaagca aatgctatct acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180  
attaaatatg tctgacttct tttgagggtc cacgactagg caaatgctat ttacgatctg 240  
caaaagctgt ttgaagagtc aaagccccc tgtgaacacg atttctggac cctgtaacag 300  
t 301

<210> 286  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 286  
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60  
tgtatattat ttttgctta cagtggatca ttctagtagg aaaggacagt aagatttttt 120  
atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccacca 180  
aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt 240  
gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt ttttccttg 300  
t 301

<210> 287  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 287  
tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60  
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaatatg 120  
aaatgatttg gttatgaacg cacagttagg gcagcagggc cagaatcctg accctctgcc 180  
ccgtgggtat ctccctccca gcttggtgct ctcagtgtat cacagtattc cattttgttt 240  
gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc 300  
t 301

<210> 288  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 288  
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60  
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120  
gatctttaaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatac 180  
aaaagcatct gcttttgtga ttaatttag ctcactctgg cactggaaga atccaaacag 240  
tctgccttaa ttttggtatg atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300  
a 301

<210> 289  
<211> 301



<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 289  
ggtacactgt ttccatgtta tgtttctaca cattgctacc tcagtgtcc tggaaactta 60  
gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg 120  
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa 180  
cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaga 240  
tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagnnga 300  
a 301

<210> 290  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 290  
acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac 60  
tgactgatct gttcatttct ctcacagctc ttaccccaa aagcttttcc accctaagtg 120  
ttctgacctc cttttctaata cacagtaggg atagaggcag anccacctac aatgaacatg 180  
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctacgagtgc 240  
tgccctgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgag 300  
a 301

<210> 291  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 291  
caggtaccaa tttcttctat cctagaaaca tttcatttta tgttggtgaa acataacaac 60  
tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc 120  
tttactcttt tgtttatagg tgaatcacia aatgtatttt tatgtattct gtagttcaat 180  
agccatggct gtttacttca ttttaatttat ttagcataaa gacattatga aaaggcctaa 240  
acatgagctt cacttcccca ctaactaatt agcatctggt atttcttaac cgtaatgcct 300  
a 301

<210> 292  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 292

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accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc      60
tgtattaaat aatttttaag tttaaaagat aaaataccat cattttaaat gttgggtattc     120
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg      180
ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc     240
tcactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa      300
a                                                                                   301

```

```

<210> 293
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 293
ggtaccaagt gctggtgcca gcctgttacc tgttctcact gaaaagtctg gctaagtctc      60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt     120
aacacaaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaaa gctgttctgt     180
gtgagaattt tttaaaaggc tacttgata ataacccttg tcatttttaa tgtacctcgg      240
ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcgagcat      300
g                                                                                   301

```

```

<210> 294
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 294
tgaccataaa caatatacac tagctatctt tttaactgtc catcattagc accaatgaag      60
attcaataaaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag     120
tttaactata gtcacaganc ttaaataatc acattgtttt ctatgtctac tgaaaataag      180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc     240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt      300
t                                                                                   301

```

```

<210> 295
<211> 305
<212> DNA
<213> Homo sapien

```

```

<400> 295
gtactctttc tctccctccc tctgaattta attctttcaa cttgcaattt gcaaggatta      60
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac     120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga      180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggtga attggatggg      240
tctcagaacc atttcaccca gacagcctgt ttctatcctg ttaataaaat tagtttgggt      300
tctct                                                                                   305

```

```

<210> 296
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 296
aggtagctatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct      60

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cacctagtag	taaaactaaaa	ataaaactgaa	acttttatgga	atctgaagtt	atttttccttg	120
attaaataga	attaataaac	caatatgagg	aaacatgaaa	ccatgcaatc	tactatcaac	180
tttgaaaaag	tgattgaacg	aaccacttag	ctttcagatg	atgaacactg	ataagtcatt	240
tgtcattact	ataaatttta	aaatctgtta	ataagatggc	ctatagggag	gaaaaagggg	300
c						301

&lt;210&gt; 297

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(300)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 297

actgagtttt	aactggacgc	caagcaggca	aggctggaag	gttttgctct	ctttgtgcta	60
aaggttttga	aaaccttgaa	ggagaatcat	tttgacaaga	agtacttaag	agtctagaga	120
acaaagangt	gaaccagctg	aaagctctcg	ggggaanctt	acatgtgttg	ttaggcctgt	180
tccatcattg	ggagtgcact	ggccatccct	caaaatttgt	ctgggctggc	ctgagtggtc	240
accgcacctc	ggccgcgacc	acgctaagcc	gaattctgca	gatatccatc	acactggcgg	300

&lt;210&gt; 298

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 298

tatggggttt	gtcacccaaa	agctgatgct	gagaaaggcc	tccctggggc	ccctcccgcg	60
ggcatctgag	agacctggtg	ttccagtggt	tctggaaatg	ggtcccagtg	ccgccggctg	120
tgaagctctc	agatcaatca	cgggaagggc	ctggcgggtg	tggccacctg	gaaccaccct	180
gtcctgtctg	tttacatttc	actaycaggt	tttctctggg	cattacnatt	tgttccccta	240
caacagtgac	ctgtgcattc	tgctgtggcc	tgctgtgtct	gcaggtggct	ctcagcgagg	300
t						301

&lt;210&gt; 299

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 299

gttttgagac	ggagtttcac	tcttggtgcc	cagactggac	tgcaatggca	gggtctctgc	60
tcactgcacc	ctctgcctcc	cagggttcgag	caattctcct	gcctcagcct	cccaggtagc	120
tgggattgca	ggctcacgcc	accataccca	gctaattttt	ttgtattttt	agtagagacg	180
gagtttcgcc	atggttgcca	gctgggtctca	aactcctgac	ctcaagegac	ctgcctgcct	240
cggcctccca	aagtgtctga	attataggca	tgagtcaaca	cgccagcct	aaagatattt	300
t						301

&lt;210&gt; 300

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<400> 300  
 attcagtttt atttgctgcc ccagtatctg taaccaggag tgccacaaaa ttttgccaga 60  
 tatgtccccc acccactggg aaaggctccc acctggctac ttcctctatc agctgggtca 120  
 gctgcattcc acaaggttct cagcctaata agtttacta cctgccagtc tcaaaactta 180  
 gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttggtac 240  
 tataaagcct gcctctaaca gtccttgctt cttcacacca atcccagcgc catcccccat 300  
 g 301

<210> 301  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 301  
 ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc 60  
 agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt 120  
 gggaaactcac aaagaccctc agagctgaga caccacacac agtgggagct cacaaagacc 180  
 ctgagagctg agacacccac aacagtggga gtcacaaaag accctcagag ctgagacacc 240  
 cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt 300  
 t 301

<210> 302  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 302  
 aggtacacat ttagcttgtg gtaaatagact cacaaaactg attttaaaat caagttaatg 60  
 tgaattttga aaattactac ttaattcctaa ttcacaataa caatggcatt aaggtttgac 120  
 ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg 180  
 ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240  
 caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg 300  
 g 301

<210> 303  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 303  
 aggtaccaac tgtggaaata ggtagaggat cattttttct tccatatca actaagtgtg 60  
 atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac 120  
 tggctaattg aactaccgct tgcattgtta aaatgggtgt ttgtgaaatg atcataggcc 180  
 agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc 240  
 catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac 300  
 c 301

<210> 304  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 304  
 acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgcctaata 60  
 tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc 120  
 ctttttagtg tatcatatca ggaatcatct cacattgggt tgtgccatta ctggtgcagt 180  
 gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga 240

ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct 300  
c 301

<210> 305  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 305  
gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag 60  
cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggag 120  
taaaggagga gaaacagata caaatctcc aactcagtat taaggatttc tcatgcctag 180  
aatattggta gaaacaagaa tacattcata tggcaataa ctaaccatgg tggaacaaaa 240  
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag 300  
a 301

<210> 306  
<211> 8  
<212> PRT  
<213> Homo sapien

<400> 306  
Val Leu Gly Trp Val Ala Glu Leu  
1 5

<210> 307  
<211> 637  
<212> DNA  
<213> Homo sapien

<400> 307  
acagggratg aagggaagag gagaggatga ggaagccccc ctggggattt ggtttggtcc 60  
ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa ataggggcac 120  
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt 180  
cacaccattg gtgagggagg gattaccacc ctgggggttat gaagatgggt gaacacccca 240  
cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga 300  
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg 360  
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgggg caaactctga 420  
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtga 480  
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatatag gaagtagcca 540  
gggtgggagcc tttccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg 600  
ttacagatac tggggcagca aataaaactg aatcttg 637

<210> 308  
<211> 647  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(647)  
<223> n = A,T,C or G

<400> 308  
 acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac 60  
 tgctcagggg aaggttcata tgggactttc tactgcccaa gggtctatac aggatataaa 120  
 ggngcctcac agtataagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg 180  
 ccacccctct gacccttttg aactcctctg accctttaga acaagcctac ctaatatctg 240  
 ctagagaaaa gaccaacaac ggctcctcagg gatctcttac catgaaggctc tcagctaatt 300  
 cttgggctaag atgtgggttc cacattagggt tctgaatatg gggggaagggt tcaatttgct 360  
 catttttgtgt gtggataaaag tcaggatgcc caggggccag agcagggggc tgcttgcttt 420  
 gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac 480  
 tgtatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca 540  
 ggaccagttt gaggggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc 600  
 aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt 647

<210> 309  
 <211> 460  
 <212> DNA  
 <213> Homo sapien

<400> 309  
 actttatagt ttaggctgga cattggaaaa aaaaaaagc cagaacaaca tgtgatagat 60  
 aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg 120  
 gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc 180  
 accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtcag 240  
 ggggaattta ttccctggcaa ttttaattgg actccttatg tgagagcagc ggctaccagc 300  
 ctgggggtggt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc 360  
 acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat 420  
 ttgtcttggt tttgtctttc ggtgtgtaag attcttaagt 460

<210> 310  
 <211> 539  
 <212> DNA  
 <213> Homo sapien

<400> 310  
 acgggactta tcaataaaag ataggaaaag aagaaaactc aaatattata ggcagaaatg 60  
 ctaaaggttt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt 120  
 taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa 180  
 gtcagacagt aagatttggt ggaaatgggt tggtttggtg tatggtatgt attttagcaa 240  
 taatctttat ggcagagaaa gctaaaatcc tttagcttgc gtgaatgatc acttgctgaa 300  
 ttctcaagg taggcatgat gaaggagggt tttagaggaga cacagacaca atgaactgac 360  
 ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc acactgtgac 420  
 atgattatgt cattacatgt atggtagtga tggggatgat aggaagggaag aacttatggc 480  
 atattttcac cccacaaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga 539

<210> 311  
 <211> 526  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1) ... (526)  
 <223> n = A,T,C or G

<400> 311  
 caaatttgag ccaatgacat agaattttac aaatcaagaa gcttattctg gggccatttc 60  
 ttttgacgtt ttctctaaac tactaaagag gcattaatga tccataaatt atattatcta 120  
 catttacagc atttaaaatg tggtcagcat gaaatattag ctacagggga agctaaataa 180

atataacatg	gaataaagat	ttgtccttaa	atataatcta	caagaagact	ttgatatttg	240
tttttcacaa	gtgaagcatt	cttataaagt	gtcataacct	ttttggggaa	actatgggaa	300
aaaatgggga	aactctgaag	ggttttaagt	atcttacctg	aagctacaga	ctccataacc	360
tctctttaca	gggagctcct	gcagccccta	cagaaatgag	tggctgagat	tcttgattgc	420
acagcaagag	cttctcatct	aaaccctttc	cctttttagt	atctgtgtat	caagtataaa	480
agttctataa	actgtagtnt	acttatttta	atccccaag	cacagt		526

&lt;210&gt; 312

&lt;211&gt; 500

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(500)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 312

cctctctctc	cccacccct	gactctagag	aactgggttt	tctcccagta	ctccagcaat	60
tcattttctga	aagcagttga	gccactttat	tccaaagtac	actgcagatg	ttcaaactct	120
ccattttctct	ttcccttcca	cctgccagtt	ttgctgactc	tcaacttgct	atgagtgtaa	180
gcattaagga	cattatgctt	cttcgattct	gaagacaggc	cctgctcatg	gatgactctg	240
gcttcttagg	aaaatatttt	tcttccaaaa	tcagtaggaa	atctaaactt	atccccctct	300
tgcagatgct	tagcagcttc	agacatttgg	ttaagaacct	atgggaaaaa	aaaaaatcct	360
tgctaattgt	gtttcctttg	taaaaccanga	ttcttatttg	nctggtatag	aatatcagct	420
ctgaacgtgt	ggtaaagatt	tttgtgtttg	aatataggag	aatcagttt	gctgaaaagt	480
tagtcttaat	tatctattgg					500

&lt;210&gt; 313

&lt;211&gt; 718

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(718)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 313

ggagatttgt	gtggtttgca	gccgagggag	accaggaaga	tctgcatggt	gggaaggacc	60
tgatgataca	gaggtgagaa	ataagaaagg	ctgctgactt	taccatctga	ggccacacat	120
ctgctgaaat	ggagataatt	aacatcacta	gaaacagcaa	gatgacaata	taatgtctaa	180
gtagtgacat	gtttttgcac	atttccagcc	cttttaaata	tccacacaca	caggaagcac	240
aaaaggaagc	acagagatcc	ctgggagaaa	tgcccggccg	ccatcttggg	tcacgatga	300
gcctcgccct	gtgcctgntc	ccgcttgtga	gggaaggaca	ttagaaaatg	aattgatgtg	360
ttccttaaa	gatggcagga	aaacagatcc	tgttgtggat	atttatttga	acgggattac	420
agatttgaaa	tgaagtcaca	aagtgagcat	taccaatgag	aggaaaacag	acgagaaaat	480
cttgatgggt	cacaagacat	gcaacaaaca	aaatggaata	ctgtgatgac	acgagcagcc	540
aactggggag	gagataccac	ggggcagagg	tcaggattct	ggccctgctg	cctaactgtg	600
cgttatacca	atcatttcta	tttctaccct	caaacaagct	gtngaataatc	tgacttacgg	660
ttcttntggc	ccacattttc	atnatccacc	centcntttt	aannttante	caaantgt	718

&lt;210&gt; 314

&lt;211&gt; 358

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 314

taagattggg tttatgtgat tttagtgggt a 151

<210> 320  
<211> 150  
<212> DNA  
<213> Homo sapien

<400> 320  
aactagtgga tccactagtc cagtgtggtg gaattccatt gtgttgggt tctagatcgc 60  
gagcggctgc cctttttttt tttttttttg ggggggaatt tttttttttt aatagttatt 120  
gagtgttcta cagcttacag taaataccat 151

<210> 321  
<211> 151  
<212> DNA  
<213> Homo sapien

<400> 321  
agcaactttg tttttcatcc aggttatattt aggccttagga tttcctctca cactgcagtt 60  
taggggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg 120  
tgcctctgag aaatcaaagt cttcatacac t 151

<210> 322  
<211> 151  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(151)  
<223> n = A,T,C or G

<400> 322  
atccagcatc ttctcctggt tcttgccctc ctttttcttc ttcttasatt ctgcttgagg 60  
tttgggcttg gtcagtttgc cacagggctt ggagatgggt acagtcttct ggcattcggc 120  
attgtgcagg gctcgttca naattccagt t 151

<210> 323  
<211> 151  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(151)  
<223> n = A,T,C or G

<400> 323  
tgaggacttg tkttcttttt ctttattttt aatcctctta ckttgtaa atattgccta 60  
nagactcant tactaccag tttgtggtt twtggggagaa atgtaactgg acagttagct 120  
gttcaatyaa aaagacactt ancccatgtg g 151

<210> 324  
<211> 461  
<212> DNA  
<213> Homo sapien

<220>



&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(461)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 324

acctgtgtgg	aatttcagct	ttcctcatgc	aaaaggattt	tgtatccccg	gcctacttga	60
agaagtgggc	agctaaagga	atccagggtg	ttgggtggac	tgtaataacc	tttgatgaaa	120
agagttacta	cgaatcccat	cttggttcca	gctatatcac	tgacagcatg	gtagaagact	180
gcgaacctca	cttctagact	ttcacgggtg	gacgaaacgg	gttcagaaac	tgccaggggc	240
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cacacaaatg	caatagtgtg	tactgcatt	tttacctgaa	ccaaagctaa	acccggtgtt	360
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&lt;210&gt; 325

&lt;211&gt; 400

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 325

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&lt;210&gt; 326

&lt;211&gt; 1215

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 326

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&lt;210&gt; 327

&lt;211&gt; 220

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 327

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Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met
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Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
          20           25           30
Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
          35           40           45
Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
          50           55           60
Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
          65           70           75           80
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
          85           90           95
Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
          100          105          110
Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
          115          120          125
Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
          130          135          140
Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
          145          150          155          160
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
          165          170          175
Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
          180          185          190
Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
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Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
          210          215          220

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&lt;210&gt; 328

&lt;211&gt; 234

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 328

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atccgcagtg ggtgctgtca gccacacact gtttcagaaa ctccacacc atcgggctgg      180
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&lt;210&gt; 329

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 329

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          20           25           30
Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
          35           40           45
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<213> Homo sapien

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<212> PRT  
<213> Homo sapien

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Val Ser Gly Ser Cys Ser  
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<213> Homo sapien

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 <212> DNA  
 <213> Homo sapien

<400> 333

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&lt;211&gt; 2417

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 334

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 <212> PRT  
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 Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln  
 35 40 45  
 Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala  
 50 55 60  
 Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln  
 65 70 75 80  
 Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln  
 85 90 95  
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 100 105 110  
 Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn  
 115 120 125  
 Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro  
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 Ala Phe Trp  
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<210> 337  
 <211> 9  
 <212> PRT  
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<400> 337  
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<400> 338  
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 1 5

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 <211> 318  
 <212> PRT  
 <213> Homo sapien

<400> 339  
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<211> 483
<212> DNA
<213> Homo sapien
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<211> 344
<212> DNA
<213> Homo sapien
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&lt;400&gt; 341

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attaatttaa	taattttctga	tgatgggttt	atctgcagta	atatgtatat	catctattag	240
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&lt;210&gt; 342

&lt;211&gt; 592

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 342

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cccggtgctc	tatgcaaata	atcgtcttct	tctaaatttc	tcctaggctt	cattttccaa	480
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&lt;210&gt; 343

&lt;211&gt; 382

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 343

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&lt;210&gt; 344

&lt;211&gt; 536

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 344

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&lt;210&gt; 345

&lt;211&gt; 251

<212> DNA  
<213> Homo sapien

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gcgtggggcca ggaaatcaca tcctacactg cccaggagcc agacacattt atggaacaga 180  
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<210> 346  
<211> 282  
<212> DNA  
<213> Homo sapien

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<223> n = A,T,C or G

<400> 346  
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agaaaggctt tctatttcac tggcccagggt agggggaagg agagtaactt tgagtctgtg 240  
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<211> 201  
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<220>  
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tctgagactg actggacca cccagacca gggcaaagat acatgttacc atatcatctt 180  
tataaagaat tttttttgt c 201

<210> 348  
<211> 251  
<212> DNA  
<213> Homo sapien

<400> 348  
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aggagacact cccagcatgg aggagggttt atcttttcat cctaggtcag gtctacaatg 180  
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gccctgcctc c 251

<210> 349  
<211> 251  
<212> DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 349

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actcctggtt	t					251

&lt;210&gt; 350

&lt;211&gt; 908

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 350

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&lt;210&gt; 351

&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 351

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&lt;210&gt; 352

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 352

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<210> 355  
 <211> 676  
 <212> DNA  
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<212> DNA  
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<212> DNA  
<213> Homo sapien

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atagatatata ttattccagt ttttttaaaa cttaaaarat attccattgc cgaattaara 240  
araarataag tggtatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa 300  
gcataatctg tacaaaatta aactgtcctt tttggcattt taacaaattt gcaacgktct 360  
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<213> Homo sapien

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<213> Homo sapien

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<210> 363  
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 <212> DNA  
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<220>  
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&lt;210&gt; 364

&lt;211&gt; 401

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 364

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&lt;210&gt; 365

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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 365

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&lt;210&gt; 366

&lt;211&gt; 1851

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 366

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&lt;210&gt; 367

&lt;211&gt; 668

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 367

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&lt;211&gt; 1512

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 368

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&lt;210&gt; 369

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 369

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&lt;210&gt; 370

&lt;211&gt; 2184

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 370

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gttgacgtga gccgagatcc gccactacac tccagcctgg gtgacagagc aagactctgt      2160
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&lt;210&gt; 371

&lt;211&gt; 1855

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(1855)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 371

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cgtaacggct tggctgccct gtaacggctt gcacgtgcat gctgcacgcg cggttaacggc      240
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tcttggattg acgttctctc cttggatkga cgtttctctc ttggatkga gtttctytyt      360

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ctggctgtta	aaagcagatg	gtggctgagg	ttgattcaat	gccggctgct	tcttctgtga	720
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&lt;210&gt; 372

&lt;211&gt; 1059

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 372

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&lt;210&gt; 373

&lt;211&gt; 1155

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 373

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tatggtgctg	atatcgaatc	aaaaaacaag	catggcctca	caccactgtt	acttgggtgta	840
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gccagagagt	atgctgtttc	tagtcatcat	catgtaattt	gccagttact	ttctgactac	1080
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accagaaata	aataa					1155

&lt;210&gt; 374

&lt;211&gt; 2000

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 374

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attctgattc	atgaagaaaa	gcagatagaa	gtgggtgaaa	aaatgaattc	tgagcttctc	1860
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<210> 375  
 <211> 2040  
 <212> DNA  
 <213> Homo sapien

<400> 375  
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 agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag 180  
 atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaacgtg 240  
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 gagctagaca caatgaaaca tcagagccag ctaaaaaaaa aaaaaaaaaa aaaaaataa 2040

<210> 376  
 <211> 329  
 <212> PRT  
 <213> Homo sapien

<400> 376  
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 20 25 30  
 Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser  
 35 40 45  
 Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg  
 50 55 60

```

Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
65              70              75              80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
              85              90              95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
              100              105              110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
              115              120              125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
              130              135              140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
145              150              155              160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
              165              170              175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
              180              185              190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
              195              200              205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
              210              215              220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
225              230              235              240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
              245              250              255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
              260              265              270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
              275              280              285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
290              295              300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
305              310              315              320
Ser Met Leu Phe Leu Val Ile Ile Met
              325

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&lt;210&gt; 377

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(148)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 377

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Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
              20              25              30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
              35              40              45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
50              55              60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
65              70              75              80
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
              85              90              95

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Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro  
 100 105 110  
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp  
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 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser  
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 Lys Asn Lys Val  
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<210> 378  
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 <212> PRT  
 <213> Homo sapien

<400> 378  
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 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val





tgagcagatg gtttctgagg acgt

384

<210> 395

<211> 399

<212> DNA

<213> Homo sapiens

<400> 395

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gcagcctgggt gagaccatcc aatcccaaat aaaatgcac 399
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<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

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agacaaggac aacctgttcc ttcat'aactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaaa gtggatgaat aatctggata ttttctctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gttttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
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<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397

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tccatccccg ctcttggttg gtnacagaat gactgacaaa 100
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<210> 398

<211> 278

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(278)

<223> n = A,T,C or G

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			820					825					830		
Gly	Leu	Ile	Pro	Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe
		835					840					845			
Pro	Asp	Asn	Glu	Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser
	850					855					860				
Asp	Tyr	Lys	Glu	Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn
865					870					875					880
Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu
			885						890					895	
Glu	Gly	Ser	Glu	Asn	Gly	Gln	Pro	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile
			900					905					910		
Glu	Glu	Met	Lys	Lys	His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn
	915						920					925			
Leu	Thr	Asn	Gly	Ala	Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro
	930						935					940			
Pro	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu
945					950					955					960
Asn	Glu	Glu	Tyr	His	Ser	Asp	Glu	Gln	Asn	Asp	Thr	Gln	Lys	Gln	Phe
				965					970					975	
Cys	Glu	Glu	Gln	Asn	Thr	Gly	Ile	Leu	His	Asp	Glu	Ile	Leu	Ile	His
			980					985					990		
Glu	Glu	Lys	Gln	Ile	Glu	Val	Val	Glu	Lys	Met	Asn	Ser	Glu	Leu	Ser
		995					1000					1005			
Leu	Ser	Cys	Lys	Lys	Glu	Lys	Asp	Ile	Leu	His	Glu	Asn	Ser	Thr	Leu
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Arg	Glu	Glu	Ile	Ala	Met	Leu	Arg	Leu	Glu	Leu	Asp	Thr	Met	Lys	His
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Gln	Ser	Gln	Leu	Pro	Arg	Thr	His	Met	Val	Val	Glu	Val	Asp	Ser	Met
				1045					1050					1055	
Pro	Ala	Ala	Ser	Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met
			1060					1065					1070		
Gly	Lys	Trp	Cys	Cys	Arg	Cys	Phe	Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys
		1075					1080					1085			
Ser	Asn	Val	Gly	Thr	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr
	1090						1095					1100			
Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys	Arg	His	Cys	Phe	Pro	Cys	Cys
1105					1110						1115				1120
Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val	Gly	Ala	Ser	Gly	Asp	His	Asp	Asp
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Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn	Lys	Met	Gly	Lys	Trp	Cys	Cys	His
			1140					1145					1150		
Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp
		1155					1160					1165			
Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe	Met	Glu	Pro	Arg	Tyr	His	Val	Arg
	1170						1175					1180			
Gly	Glu	Asp	Leu	Asp	Lys	Leu	His	Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val
1185					1190					1195					1200
Pro	Arg	Lys	Asp	Leu	Ile	Val	Met	Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys
				1205					1210					1215	
Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala	Leu	His	Leu	Ala	Ser	Ala	Asn	Gly
			1220					1225					1230		
Asn	Ser	Glu	Val	Val	Lys	Leu	Leu	Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn
		1235					1240					1245			
Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr	Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys
	1250					1255					1260				
Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met	Leu	Leu	Glu	His	Gly	Thr	Asp	Pro

1265	1270	1275	1280
Asn Ile Pro Asp	Glu Tyr Gly Asn Thr	Thr Leu His Tyr Ala Ile Tyr	
1285	1290	1295	
Asn Glu Asp Lys	Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp		
1300	1305	1310	
Ile Glu Ser Lys	Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val		
1315	1320	1325	
His Glu Gln Lys	Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala		
1330	1335	1340	
Asn Leu Asn Ala	Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala		
1345	1350	1355	1360
Val Cys Cys Gly	Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn		
1365	1370	1375	
Ile Asp Val Ser	Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr		
1380	1385	1390	
Ala Val Ser Ser	His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr		
1395	1400	1405	
Lys Glu Lys Lys	Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu		
1410	1415	1420	
Gln Asp Leu Lys	Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly		
1425	1430	1435	1440
Ser Glu Asn Ser	Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn		
1445	1450	1455	
Lys Asp Gly Asp	Arg Glu Val Glu Glu Met Lys Lys His Glu Ser		
1460	1465	1470	
Asn Asn Val Gly	Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly		
1475	1480	1485	
Asn Gly Asp Asn	Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu		
1490	1495	1500	
Asn Gln Gln Phe	Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys		
1505	1510	1515	1520
Glu Leu Val Ser	Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser		
1525	1530	1535	
Glu Asn Ser Asn	Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu		
1540	1545	1550	
Ser Gln Arg Leu	Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser		
1555	1560	1565	
Gln Glu Pro Glu	Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe		
1570	1575	1580	
Met Ala Ile Glu	Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe		
1585	1590	1595	1600
Pro Glu Asn Leu	Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly		
1605	1610	1615	
Leu Ile Pro Pro	Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro		
1620	1625	1630	
Asp Thr Glu Asn	Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln		
1635	1640	1645	
Lys Gln Phe Cys	Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile		
1650	1655	1660	
Leu Ile His Glu	Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser		
1665	1670	1675	1680
Glu Leu Ser Leu	Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn		
1685	1690	1695	
Ser Thr Leu Arg	Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr		
1700	1705	1710	
Met Lys His Gln	Ser Gln Leu		
1715			

<210> 379  
 <211> 656  
 <212> PRT  
 <213> Homo sapien

<400> 379  
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 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu  
 370 375 380  
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys  
 385 390 395 400  
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu  
 405 410 415

Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn  
                   420                  425                  430  
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro  
                   435                  440                  445  
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu  
                   450                  455                  460  
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu  
                   465                  470                  475                  480  
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp  
                   485                  490                  495  
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu  
                   500                  505                  510  
 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys  
                   515                  520                  525  
 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly  
                   530                  535                  540  
 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser  
                   545                  550                  555                  560  
 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr  
                   565                  570                  575  
 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln  
                   580                  585                  590  
 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln  
                   595                  600                  605  
 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys  
                   610                  615                  620  
 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile  
                   625                  630                  635                  640  
 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu  
                   645                  650                  655

&lt;210&gt; 380

&lt;211&gt; 671

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 380

Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
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 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
                   20                  25                  30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
                   35                  40                  45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
                   50                  55                  60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
                   65                  70                  75                  80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
                   85                  90                  95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
                   100                  105                  110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
                   115                  120                  125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
                   130                  135                  140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
                   145                  150                  155                  160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala



625                      630                      635                      640  
 Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala  
                                  645                      650                      655  
 Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu  
                                  660                      665                      670

<210> 381  
 <211> 251  
 <212> DNA  
 <213> Homo sapien

<400> 381  
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 ccaatatccc aggagaagca ttggggaggt gggggcaggt gaaggaccca ggactcacac 180  
 atcctgggcc tccaaggcag aggagaggggt cctcaagaag gtcaggagga aaatccgtaa 240  
 caagcagtca g 251

<210> 382  
 <211> 3279  
 <212> DNA  
 <213> Homo sapiens

<400> 382  
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 atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120  
 cactgggagg ggacatcctg cagaaggtag gagtgcagca acacccgctg caggggaggg 180  
 gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ctgggaggag 240  
 gggcctggag ggcgtgagga ggagcgaggg ggctgcatgg ctggagttag ggatcagggg 300  
 cagggcgcgga gatggcctca cacaggggaag agagggcccc tcctgcaggg cctcacctgg 360  
 gccacaggag gacactgctt ttcctctgag gagtgcaggag ctgtggatgg tgctggacaa 420  
 aagaaggaca gggcctggct cagggtgtcca gaggctgtcg ctggcttccc tttgggatca 480  
 gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540  
 gtggctccag gccttgcccc tgctggggcc ctcaccagc ctccctcaca gtctcctggc 600  
 cctcagtctc tccccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660  
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 ggacatctag tcagagagta gtccctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780  
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 agagatggag ttgcctaggc agttattggg gccaatcttt ctactgtgt ctctcctcct 1080  
 ttacccttag ggtgattctg ggggtccact tgtctgtaat ggtgtgcttc aaggtatcac 1140  
 atcatggggc cctgagccat gtgccctgcc tgaaaagcct gctgtgtaca ccaagtggt 1200  
 gcattaccgg aagtggatca aggacacat cgagcccaac ccctgagtgc ccctgtccca 1260  
 cccctacctc tagtaaat ttagtccacct cacgttctgg catcacttgg cctttctgga 1320  
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 ctagataagg ccgtgagcag aaagaagggg aggatcctcc tatgttgttg aaggagggac 1800  
 tagggggaga aactgaaagc tgattaatta caggaggttt gttcaggtcc cccaaaccac 1860  
 cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggt 1920  
 ttattatggt ttgttacatt gataggatac atactgaaat cagcaaacaa aacagatgta 1980  
 tagattagag tgtggagaaa acagaggaaa acttgcagtt acgaagactg gcaacttggc 2040

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gttatgaaga tggttgaaca cccacacat agcaccggag atatgagatc aacagtttct 2880
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acaagacggg ggggcaaact ctgatttccg tgggggaatg tcatggtctt gctttactaa 3060
gttttgagac tggcaggtag tgaactcat taggctgaga accttgtgga atgcagctga 3120
cccagctgat agaggaagta gccaggtggg agcctttccc agtgggtgtg ggacatatct 3180
ggcaagattt tgtggcactc ctggttacag atactggggc agcaaataaa actgaatctt 3240
gttttcagac cttaaaaaaa aaaaaaaaaa aaaagtctt 3279

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&lt;210&gt; 383

&lt;211&gt; 154

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 383

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Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
      5                      10                      15

Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
      20                      25                      30

His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35                      40                      45

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50                      55                      60

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65                      70                      75                      80

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85                      90                      95

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100                     105                     110

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
      115                     120                     125

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
      130                     135                     140

Ala Leu Glu Arg Gly His Leu Val Arg Glu
      145                     150

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<210> 384  
<211> 557  
<212> DNA  
<213> Homo sapiens

<400> 384  
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aaagatgtgt tttgttttgg actctctgtg gtcccttcca atgctgtggg tttccaacca 120  
ggggaagggt cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggt 180  
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240  
acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300  
ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360  
tccccaaagac acatcctaaa aggtgttgta atgggtgaaa cgtcttcctt ctttattgcc 420  
ccttccttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480  
tcaattgtga aaatgaatat catgcaaata aattatgcga tttttttttc aaagtaaaaa 540  
aaaaaaaaaa aaaaaaa 557

<210> 385  
<211> 337  
<212> DNA  
<213> Homo sapiens

<400> 385  
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gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120  
tctcaaagcc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180  
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240  
tatcagacag gtccagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct 300  
ctttggccac caattcccc tttccacat cccggca 337

<210> 386  
<211> 300  
<212> DNA  
<213> Homo sapiens

<400> 386  
gggcccgccta ccggcccagg cccgcctcgc cgagtcctcc tccccgggtg cctgcccgcga 60  
gcccgcctcgc ccagaggggt ggcgcgggg ctgcctctac cggttgccgg ctgtaactca 120  
gcgaccttg cccgaaggct ctagcaagga ccaccgacc ccagccgcgg cggcggcgcc 180  
gcggactttg cccggtgtgt gggcgaggc ggactgcgtg tccgcggacg ggcagcgaag 240  
atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

<210> 387  
<211> 537  
<212> DNA  
<213> Homo sapiens

<400> 387  
gggcccagtc gggcaccaag ggactctttg caggcttcct tcctcggatc atcaaggctg 60  
ccccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120  
tgaaccagga ccggtctctg ggcggctgaa aggggcaagg aggcaaggac cccgtctctc 180  
ccacggatgg ggagagggca ggaggagacc cagccaagtg ctttttcctc agcactgagg 240  
gagggggcct gtttcccttc cctcccggcg acaagctcca gggcagggct gtccctctgg 300  
gcggcccagc acttctcag acacaacttc ttctgctgc tccagtcgtg gggatcatca 360  
cttaccacc ccccaagttc aagaccaaact cttccagctg ccccttcgt gtttccctgt 420  
gtttgtctgta gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg ttagtctcc 480  
ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaa aaaaaaa 537

<210> 388  
 <211> 520  
 <212> DNA  
 <213> Homo sapiens

<400> 388  
 aggataat ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60  
 tgagggttaa ccagtttgca ttccccta atgtggaaaa taagaggact actcagcact 120  
 gtttgaagat tgcctcttct acagcttctg agaatttgtt tatttcactt gccaagtga 180  
 ggacccccct cccaacatgc ccagccccc ccctaagcat ggtcccttgt caccaggcaa 240  
 ccaggaaact gctacttgtg gacctcacca gagaccagga ggggttgggt agctcacagg 300  
 acttccccca cccagaaga ttagcatccc atactagact cataactcaac tcaactagga 360  
 tcatactcaa ttgatgggta ttagacaatt ccatttcttt ctgggtatta taaacagaaa 420  
 atctttcctc ttctcattac cagtaaaggc tcttgggtatc tttctgttgg aatgatttct 480  
 atgaacttgt cttattttaa tggtaggggt ttttcttgt 520

<210> 389  
 <211> 365  
 <212> DNA  
 <213> Homo sapiens

<400> 389  
 cgttgcccca gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60  
 gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctcccc 120  
 aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180  
 aagcctatgg ccagctgtct ttgtgttccc tctcaccgc ctgtcctcac agctgagact 240  
 ccaggaaac cttcagacta ccttcctctg cttcagcaa ggggcgttg ccacattctc 300  
 tgagggtcag tgaagaacc tagactccca ttgctagagg tagaaaggga aagggtgctg 360  
 gggag 365

<210> 390  
 <211> 221  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(221)  
 <223> n = A,T,C or G

<400> 390  
 tgctcttcca tcctggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60  
 tacacggnnt ctcattgggtg tgaacatct ctgcttgagg ttccaggaag gcctctggct 120  
 gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180  
 tcaaagtcta gagggagtgg aggagttaag gctggatttc a 221

<210> 391  
 <211> 325  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(325)  
 <223> n = A,T,C or G

<400> 391

```

tggagcaggt cccgagggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctacca caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naanttn gat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgcccag gaatcctaca gccagtaccc tgtcccgacg tctctaccta ccagtacgat 300
gagacctccg gctactacta tgacc 325

```

<210> 392

<211> 277

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1) ... (277)

<223> n = A,T,C or G

<400> 392

```

atattgttta actccttctt ttatatcttt taacattttc atggngaaag gtccacatct 60
agtctcactt ngcnagn gn ctctacttg agtctcttcc ccggcctggn ccagtnngaa 120
antaccanga accgncatgn cttaanaacn ncctggtttn tgggttnntc aatgactgca 180
tgcaagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa 277

```

<210> 393

<211> 566

<212> DNA

<213> Homo sapiens

<400> 393

```

actagtcacag tgtggtggaa ttcgcgcccg cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga ttaaattcag cctaaacggt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
gagaaggtct agtttgcca tcagcattat catgatata ggactggtta cttgggttaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttgga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcacctgta aacattttat 360
catttattaa tcacctctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
ttctgcctca atgtttactg tgcctttggt tttgctagtt tgtgtgtgtg aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540
ttttgcctat caaaaaaaaa aaaaaa 566

```

<210> 394

<211> 384

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1) ... (384)

<223> n = A,T,C or G

<400> 394

```

gaacatacat gtcccgccac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaatng gaccgggcca aggtggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttta ggagttttta gctgagtgtc actgtagacc ccaaatacca 180
tcccaagatt atcgggagaa agggggcagt aattacccaa atccggttg agcatgacgt 240
gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaa ttaccatcac 300
aggttacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360

```

<400> 398  
 ggggcccgt cgacagcagt tccgccagcg ctgcccctg ggtggggatg tgctgcacgc 60  
 ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120  
 tctactctgt gcctcgacca gtgaggagag ctggaccgac agcgaggtgg actcatcatg 180  
 ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240  
 ctatggccgc ttcat tangt ggctcaacaa ggagaagg 278

<210> 399  
 <211> 298  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(298)  
 <223> n = A,T,C or G

<400> 399  
 acggaggtgg aggaagcgc cctgggatcg anaggatggg tcctgncatt gaccnccctn 60  
 ggggtgccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120  
 ccgagatcga gcgcatgggc ctggatcatgg accgcatggg ctccgtggag cgcgtgggct 180  
 ccggcattga gcgcatgggc ccgctgggccc tcgaccacat ggccctccanc attgancgca 240  
 tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg 298

<210> 400  
 <211> 548  
 <212> DNA  
 <213> Homo sapiens

<400> 400  
 acatcaacta cttcctcatt ttaaggatag gcagttccct tcateccctt ttctgcctt 60  
 gtacatgtac atgtatgaaa ttcccttctc ttaccgaact ctctccacac atcacaagg 120  
 caaagaacca cacgcttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180  
 tgagtctctt ttttccacgt ttaagggggc atggcaggac ttagagttgc gagttaagac 240  
 tgcagagggc tagagaatta ttccatacag gctttgaggc caccatgtc acttatcccg 300  
 tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360  
 gttggcccc taattctggg cctttgttgt ttgttttaac tacttgggca tccagggaag 420  
 ctttccagtg atctcctacc atgggcccc ctctgggat caagccctc ccaggccctg 480  
 tccccagccc ctctgcccc agcccacccg cttgccttgg tgctcagccc tccattggg 540  
 agcaggtt 548

<210> 401  
 <211> 355  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(355)  
 <223> n = A,T,C or G

<400> 401  
 actgtttcca tggtatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60  
 tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120  
 taagagtggg ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180  
 tataaatgaa tgtgctgaag caaagtggcc atggtggcgg cgaagaagan aaagatgtgt 240  
 tttgttttgg actctctgtg gtcccttcca atgctgnggg ttccaacca ggggaagggt 300

cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc 355

<210> 402

<211> 407

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(407)

<223> n = A,T,C or G

<400> 402

```
atgggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aatggaaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgaccttg ataatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa 407
```

<210> 403

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 403

```
cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcacccaa 60
tcctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
gga 303
```

<210> 404

<211> 225

<212> DNA

<213> Homo sapiens

<400> 404

```
aagtgttaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagtgc tctcttgatc ctacaaacag 120
acattttcca ctcggtgttc catagttggt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcatt 225
```

<210> 405

<211> 334

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

```
gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgaggggtg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
tcatccccat cccatgccaa aggaagaccc tccctccttg gtcacagcc ttctctaggg 180
ttcccagtg ctcaggaca gagggggta tgttttcagc tccatccttg ctgtgagtg 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcannn tggatcccac ccct 334
```

<210> 406

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1) ... (216)

<223> n = A,T,C or G

<400> 406

```
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant 216
```

<210> 407

<211> 413

<212> DNA

<213> Homo sapiens

<400> 407

```
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcacccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag 413
```

<210> 408

<211> 183

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1) ... (183)

<223> n = A,T,C or G

<400> 408

```
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tncttaacta gttaatcctt aaagggctan ntaatcctta actagtccct ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttcttggtta cccatgtact 180
ntt 183
```

<210> 409

<211> 250

<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(250)  
<223> n = A,T,C or G

<400> 409  
cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60  
gtgggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120  
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180  
gcttccagtg gccccagga cagcgtgggc tatgtttaca gcgctcctt gctggggggg 240  
ggcctatgc 250

<210> 410  
<211> 306  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(306)  
<223> n = A,T,C or G

<400> 410  
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60  
agtcttgcaa tccatttgc aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120  
cccagggacc ttggaaacag ttggcactgt aaggtgcttg ctccccaga cacatcctaa 180  
aaggtgttgt aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240  
nactggtttg ctttttttgn atctttttta aactggaaaag ttcaattgng aaaatgaata 300  
tcntgc 306

<210> 411  
<211> 261  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(261)  
<223> n = A,T,C or G

<400> 411  
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60  
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120  
tttaaattgc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180  
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240  
cttctctcaa ggngaggcaa a 261

<210> 412  
<211> 241  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(241)

<223> n = A,T,C or G

<400> 412

```
gttcaatggt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggagggggag 180
ctgggagatt tctctgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
a 241
```

<210> 413

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 413

```
aactcttaca atccaagtga ctcattctgtg tgcttgaatc ctttccactg tctcatctcc 60
ctcatccaag tttctagtag cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tctctatttg gaacctaaaa actctcttct tcttgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231
```

<210> 414

<211> 234

<212> DNA

<213> Homo sapiens

<400> 414

```
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggg cttccttttg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tgggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca 234
```

<210> 415

<211> 217

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(217)

<223> n = A,T,C or G

<400> 415

```
gcataggatt aagactgagt atcttttcta cattctttta acttttctaag gggcatttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cacttttctca 120
cacctagcaa tagtagaatt cagtccact tctgaggcca gaagaatggg tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc 217
```

<210> 416

<211> 213

<212> DNA

<213> Homo sapiens

<220>



<221> misc\_feature  
 <222> (1)...(213)  
 <223> n = A,T,C or G

<400> 416  
 atgcataatnt aaagganact gcctcgcttt tagaagacat ctggngctgct ctctgcatga 60  
 ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120  
 cgaatgcaag gtgggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180  
 atattggaac agatggagtc tctactacaa aag 213

<210> 417  
 <211> 303  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

<400> 417  
 nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60  
 gtgggaaagg ctttactctg agttcaaadc ttcaagccca tcagagagtc cacactggag 120  
 agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180  
 ttcactctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggtt 240  
 tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300  
 agt 303

<210> 418  
 <211> 328  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(328)  
 <223> n = A,T,C or G

<400> 418  
 tttttggcgg tgggtgggga gggacgggac angagtctca ctctgttgcc caggctggag 60  
 tgcacaggca tgatctcggc tcactacaac ccctgcctcc catgtccaag cgattcttgt 120  
 gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180  
 gtattttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240  
 tcagnngtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300  
 aaagtgtan gattacagga cgtgagcc 328

<210> 419  
 <211> 389  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(389)  
 <223> n = A,T,C or G

<400> 419  
 cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatag 60

```

acccttgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttgctg 120
cttgtttctt ctctgtggct ccattcatag cacagttgtt gcaactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggg gtgccaggca 240
ccggtttctc agccaccaac ctactctcgt cccgcaaagt gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg 389

```

&lt;210&gt; 420

&lt;211&gt; 408

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 420

```

gttcctccta actcctgcc aaaacagctc tctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggtt tcttgtttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtccatttga cacctttccc actgaccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgtatg acaaacctgg caagcccg 408

```

&lt;210&gt; 421

&lt;211&gt; 352

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(352)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 421

```

gctcaaaaat ctttttactg atnggcattg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacagggtc tttttgggtc cttcttctcc accacnata acttgcatc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacagggt tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcattgc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg 352

```

&lt;210&gt; 422

&lt;211&gt; 337

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 422

```

atgccaccat gctggcaatg cagcggggcg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcgcgcgcg cgtcaatcct ggccaagggt agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcgcgcgcg cataagggtc 240
atccgacacc ggtgcacctg gaagccttgc agcggtggg gccgacgcg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat 337

```

&lt;210&gt; 423

&lt;211&gt; 310

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

<221> misc\_feature  
<222> (1)...(310)  
<223> n = A,T,C or G

<400> 423  
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60  
aggagaatga ggctggcctt gggagccctg tgcctactan aagcncatta gattatccat 120  
tactgacag aacagggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180  
tccttcttga agattctttg gcagttgtct ttgtcataac ccacagggtg anaaacaagg 240  
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300  
tccgagttta 310

<210> 424  
<211> 370  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(370)  
<223> n = A,T,C or G

<400> 424  
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60  
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120  
cactgacaga acagggtctt ttttgggtcc ttcttctcca cactgatata ttgcagtcc 180  
ccttcttgaa gattcttttg cagttgtctt tgtcataacc cacagggtga gaaacatcct 240  
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300  
cacgaagggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360  
tccgtcgacg 370

<210> 425  
<211> 216  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(216)  
<223> n = A,T,C or G

<400> 425  
aattgctatn ntttattttg ccaactcaaaa taattaccaa aaaaaaaaaa tnttaaatga 60  
taacaacnca acatcaaggn aananaaca ggaatggntg actntgcata aatnggccga 120  
anattatcca ttatnttaag ggttgacttc aggttacagc acacagacaa acatgcccag 180  
gaggntntca ggaccgctcg atgtntntng aggagg 216

<210> 426  
<211> 596  
<212> DNA  
<213> Homo sapiens

<400> 426  
cttcagtgga ggataaccct gttgccccgg gccgagggtc tccattagga tctgattgat 60  
tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaaggg tcgctggcca 120  
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatgggtga 180  
gctgtccttg tattttgatt aacctaatgg cttcccagc acgactcgga ttcagctgga 240  
gacatcacgg caacttttaa tgaaatgatt tgaagggcca ttaagaggca cttcccgtta 300

```
ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtaggatggc cttttcagct ttaacccaat ttgcaactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggg cacagcagat gtcattgggc tactgcctga 540
gtcccgtctg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596
```

<210> 427

<211> 107

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(107)

<223> n = A,T,C or G

<400> 427

```
gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccag 60
cccgggagca gccttanaga gctcctgttt gactgcccgg ctcagng 107
```

<210> 428

<211> 38

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(38)

<223> n = A,T,C or G

<400> 428

```
gaacttcena anaangactt tattcactat ttacatt 38
```

<210> 429

<211> 544

<212> DNA

<213> Homo sapiens

<400> 429

```
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180
tttgatgggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
gccttcactc tcagttacac ctactcacc atcctctcct gttggttctg tgctgcttca 300
agatactaag ccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgcccttcta tgatgtcctt gatgttctca tcaagccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggtttt ttgccagggtg gtaggagaga 540
ttat 544
```

<210> 430

<211> 507

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(507)

<223> n = A,T,C or G

<400> 430

```
cttatcncaa tgggggtccc aaacttggt gtgcagtga aactccgggg gaattttgaa 60
gaacactgac acccatcttc caccgacaca ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttggt atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cnctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggg ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtga tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcttc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa 507
```

<210> 431

<211> 392

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(392)

<223> n = A,T,C or G

<400> 431

```
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggctttttac tctgctgttt ct 392
```

<210> 432

<211> 387

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(387)

<223> n = A,T,C or G

<400> 432

```
ggtatccta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattcct ttgtctataa tactgtattg 120
ngtagtccaa gctctcggna gtccagccac tngaaacat gtcctcttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tatcttgcct ctgtctgnga 240
attctgttgc ttctggggca tttccttgng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtag aggaccggga 360
acaacgtata gaacactgga gtccttt 387
```

<210> 433

<211> 281

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1) ... (281)

<223> n = A,T,C or G

<400> 433

```
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagnagg ntctctgtnt gccactgggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281
```

<210> 434

<211> 484

<212> DNA

<213> Homo sapiens

<400> 434

```
ttttaaaata agcatttagt gctcagtcct tactgagtac tctttctctc cctcctcttg 60
aatttaattc ttccaacttg caatttgcaa ggattacaca ttccactgtg atgtatattg 120
tgttgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatgggtc tcagaacccat ttcacccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttaa 484
```

<210> 435

<211> 424

<212> DNA

<213> Homo sapiens

<400> 435

```
gcgcgctca gagcagggtca ctttctgcct tccacgtcct ccttcaagga agcccatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatgggtc ggggtgaccc 240
cttgagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaacctt gaggattttc tctgttttcc actcgcaata aattcagagc 420
aaac 424
```

<210> 436

<211> 667

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1) ... (667)

<223> n = A,T,C or G

<400> 436

```
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatectga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cgggtcaacgt ctgtgcttcg aatataaacc 360
```

```

tgttcatgtt tataggactc attcaagaat tttctatatc tctttcttat atactctcca 420
agttcataat gctgctccat gccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaagggtg tcaatgggac ttcggtctcc atgccgaaac 540
accaaagtca caaacttcaa ctcttggt agtacacttc ggtctagcca gaaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttgag 667

```

&lt;210&gt; 437

&lt;211&gt; 693

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 437

```

ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggctactcct ctattttcac ccctcttgct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
cattttctcca ggttacccta ggtgtcacta ttgggggggac agccagcatc tttagctttc 420
at ttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaaact gctgttgctc ctgaggtggg gaaagacaga tatagagctt acagtattta 540
tcctattttct aggcactgag ggctgtgggg taccttgtgg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc 693

```

&lt;210&gt; 438

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 438

```

ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac ctctgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atggtttctac acctgtgggt tatgacaaag acaactgccca aagaatcttc aagaaggagg 180
actgcaagta tatctgggtg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

```

&lt;210&gt; 439

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(431)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 439

```

gttccnnta actcctgccca gaaacagctc tctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggg gtttcggcat ggagaccgaa 180
gtccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgctga cgcggccgcg 420
aatttagtag t 431

```

<210> 440  
<211> 523  
<212> DNA  
<213> Homo sapiens

<400> 440  
agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60  
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120  
tttaaattgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180  
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240  
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300  
actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360  
taaaaattaa aacctctttg tgtcccttgg tcctgggaaca tttatgttcc ttttaaagaa 420  
acaaaaatca aactttacag aaagatttga tgtatgtaac acatatagca gctcttgaag 480  
tatatatatc atagcaaata agtcactctga tgagaacaag cta 523

<210> 441  
<211> 430  
<212> DNA  
<213> Homo sapiens

<400> 441  
gttcctccta actcctgccg gaaacagctc tcctcaacat gagagctgca cccctcctcc 60  
tggccagggc agcaagcctt agccttggtc tcttggttct gcttttttcc tggctagacc 120  
gaagtgtact agccaaggag ttgaagtttg tgacttttgt gtttcggcat ggagaccgaa 180  
gtccatttga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240  
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300  
gatatagaaa attcttgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360  
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcgccgcgcg 420  
aathtagtag 430

<210> 442  
<211> 362  
<212> DNA  
<213> Homo sapiens

<400> 442  
ctaaggaatt agtagtggtc ccatcacttg tttggagtgt gctattctaa aagattttga 60  
tttcctggaa tgacaattat attttaactt tgggtgggga aagagttata ggaccacagt 120  
cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaagctat 180  
atgttttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240  
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattccttt 300  
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360  
tc 362

<210> 443  
<211> 624  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(624)  
<223> n = A,T,C or G

<400> 443  
tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60



```

ttgaaagaat taaattcaga ggaggggaga gaaagagtag tcagtaggga ctgagcacta 120
aatgcttatt ttaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccgggc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaaacttg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaataaac 360
taacgcctac aaacacttta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgcta 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaagggtt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttgggc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc 624

```

<210> 444

<211> 425

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(425)

<223> n = A,T,C or G

<400> 444

```

gcacatcatt nntcttgcatt tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgtg gtcagcaaat ccttgaatgc 180
tgcttaattg gagagggttg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcacacctg gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggctcgac cgccgcgcaa tttagtagta 420
gtaga 425

```

<210> 445

<211> 414

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 445

```

catgtttatg nttttggatt actttgggca cctagtgttt ctaaactcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcattgtgg agattattgg atgtagtctt ctttaactag catataaatc 180
tgggtgtgtt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggtctctcc tcttgatttt tgaagcagtg 360
tgggtgtctg attgataaaa aaaaaaaaag tcgacgcggc cgcgatttta gtag 414

```

<210> 446

<211> 631

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(631)

<223> n = A,T,C or G

<400> 446

```
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcagggtgtg 120
atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttgttc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtgggtggc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaactttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatggt tcacagtggc tggactaccg agagcttggg ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccctg catttgtggg 540
aatctacacc aatgaaaaca tgtactacag ctatatattga ttatgtatgg atatatattga 600
aatagtatac attgtcttga tgttttttct g 631
```

<210> 447

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(585)

<223> n = A,T,C or G

<400> 447

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gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
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attcctttat ggggtcagtg ggaaagggtg caatgggact tcggtctcca tgccgaaaca 540
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<210> 448

<211> 93

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(93)

<223> n = A,T,C or G

<400> 448

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<210> 449

<211> 706

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

&lt;222&gt; (1)...(706)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 449

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ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccttagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
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cgtacgtaag cttggatcct ctagagcggc cgcctactac tactaaattc gcggccgcgt 480
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gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaa 706

```

&lt;210&gt; 450

&lt;211&gt; 493

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 450

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acagttttta aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtgcgcaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
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tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggt cgacgcggcc 480
gcgaatttag tag 493

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&lt;210&gt; 451

&lt;211&gt; 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(501)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 451

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ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttccagc cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
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tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
cgcnccagac actcacagct actcaggagg ctgagaacag gttgaacctg ggagggtggag 420
gttgcaatga gctgagatca ggcnctgcn ccccgacatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501

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&lt;210&gt; 452

&lt;211&gt; 51

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

<220>  
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 <222> (1)...(51)  
 <223> n = A,T,C or G

<400> 452  
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<210> 453  
 <211> 317  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(317)  
 <223> n = A,T,C or G

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 ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggtc tctacatgca 180  
 taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240  
 cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300  
 taccatgtc tttatta 317

<210> 454  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 454  
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 taagccacgc cagctctctg aaggagtctt gaattctcct ctgctcactc agtagaacca 120  
 agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180  
 ccttctcttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231

<210> 455  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 455  
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 gtttcaacgc attgatgact tctccaagga tcttcttttg gcatcgacca cattcagggg 180  
 caaagaattt ctcatagcac agctcacaat acagggtctc tttctcctct a 231

<210> 456  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 456  
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 tgcactcaaa ttcctttatc aggaataact acatagccac tatttacaaa gccattggaa 180

ccttttttatt tgggtgcagct gctagtcagt ccttgactga cattgccaaag t 231

<210> 457

<211> 231

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(231)

<223> n = A,T,C or G

<400> 457

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tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180  
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<210> 458

<211> 231

<212> DNA

<213> Homo sapiens

<400> 458

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acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180  
ggtcctgggt taggcatttt ggggggccag accccaggag aagaagattc t 231

<210> 459

<211> 231

<212> DNA

<213> Homo sapiens

<400> 459

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gccctgcact gtttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180  
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a 231

<210> 460

<211> 231

<212> DNA

<213> Homo sapiens

<400> 460

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cccacctccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180  
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<210> 461

<211> 231

<212> DNA

<213> Homo sapiens

<400> 461

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gtgggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180  
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<210> 462

<211> 231

<212> DNA

<213> Homo sapiens

<400> 462

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gaagaactgt tagagagacc aacagggtag tgggttagag atttcagag tcttacattt 180  
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<210> 463

<211> 231

<212> DNA

<213> Homo sapiens

<400> 463

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catttgacag gtgtcttttc ctctggacct cggtgtcccc atctgagtga gaaaaggcag 180  
tggggagggtg gatcttccag tcgaagcggg atagaagccc gtgtgaaaag c 231

<210> 464

<211> 231

<212> DNA

<213> Homo sapiens

<400> 464

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cctgtctcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180  
ggtgccagcg caccagctag atgctctgta acttctaggc cccattttcc c 231

<210> 465

<211> 231

<212> DNA

<213> Homo sapiens

<400> 465

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taaaactggag acatgcagga cattagggta gtgttgtagc tctggtaatg a 231

<210> 466

<211> 231

<212> DNA

<213> Homo sapiens

<400> 466

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cctgtgcaat caaatattgt ggagaattcc ctagctggag aagtcacaaa gactataggc 180  
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<210> 467  
<211> 311  
<212> DNA  
<213> Homo sapiens

<400> 467  
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<210> 468  
<211> 3112  
<212> DNA  
<213> Homo sapiens

<400> 468  
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&lt;210&gt; 469

&lt;211&gt; 2229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 469

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aatggaatt

2229

&lt;210&gt; 470

&lt;211&gt; 2426

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 470

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&lt;210&gt; 471

&lt;211&gt; 812

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 471

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<210> 472

<211> 515

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

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<223> n = A,T,C or G

<400> 472

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<210> 473

<211> 5829

<212> DNA

<213> Homo sapiens

<400> 473

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aaaaaaaaa 5829

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&lt;210&gt; 474

&lt;211&gt; 1594

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 474

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&lt;210&gt; 475

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<400> 499

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<210> 500

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 500

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 1           5           10           15
Gly Ser Ile Val
                20
```

<210> 501

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 501

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 1           5           10           15
Val Ser Ala Ala
                20
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<210> 502

<211> 414

<212> DNA

<213> Homo Sapien

<220>

<221> misc\_feature

<222> (1)...(414)

<223> n = A,T,C or G

<400> 502

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<210> 503

<211> 379

<212> DNA

<211> 2414  
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<213> Homo sapiens

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3434

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<210> 477
<211> 140
<212> PRT
<213> Homo sapiens
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<400> 477
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His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr
                    20                      25                      30

Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
                    35                      40                      45

His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
                    50                      55                      60

His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
                    65                      70                      75                      80

Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
                    85                      90                      95

Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
                    100                      105                      110

Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val
                    115                      120                      125

Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
                    130                      135                      140

```

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<210> 478
<211> 143
<212> PRT
<213> Homo sapiens
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<400> 478
Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
      5                      10                      15

Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
      20                      25                      30

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
      35                      40                      45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
      50                      55                      60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
      65                      70                      75                      80

Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
      85                      90                      95

```



His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp  
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Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser  
 115 120 125

His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val  
 130 135 140

<210> 479

<211> 222

<212> PRT

<213> Homo sapiens

<400> 479

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln  
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Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr  
 20 25 30

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr  
 35 40 45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr  
 50 55 60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr  
 65 70 75 80

Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser  
 85 90 95

His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val  
 100 105 110

Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val  
 115 120 125

Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr  
 130 135 140

Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His  
 145 150 155 160

Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala  
 165 170 175

Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp  
 180 185 190

Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala  
 195 200 205

Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val  
 210 215 220

&lt;210&gt; 480

&lt;211&gt; 144

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 480

Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val  
                                   5                                  10                                  15

Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr  
                                   20                                  25                                  30

Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg  
                                   35                                  40                                  45

Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly  
                                   50                                  55                                  60

Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln  
                                   65                                  70                                  75                                  80

Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys  
                                   85                                  90                                  95

Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly  
                                   100                                  105                                  110

Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu  
                                   115                                  120                                  125

Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly  
                                   130                                  135                                  140

&lt;210&gt; 481

&lt;211&gt; 167

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 481

Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro  
                                   5                                  10                                  15

Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg  
                                   20                                  25                                  30

Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser  
                                   35                                  40                                  45

Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys  
                                   50                                  55                                  60

Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro

[illegible]

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<210> 482
<211> 143
<212> PRT
<213> Homo sapiens
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<400> 482
Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val
      5                                10                        15

Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu
      20                            25                        30

Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg
      35                          40                        45

Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly
      50                          55                        60

Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe
      65                          70                        75                        80

Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr
      85                          90                        95

Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly
      100                         105                       110

Ala Ser Gly Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys
      115                         120                       125

Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly
      130                         135                       140
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<210> 483
<211> 143
<212> PRT
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<213> Homo sapiens

<400> 483

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Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
      5              10              15

Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala
      20              25              30

Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
      35              40              45

Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
      50              55              60

Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
      65              70              75              80

Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
      85              90              95

Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
      100             105             110

Arg Leu Val Gln Ala Glu His Pro Pro Pro His Pro Leu Glu Glu Val
      115             120             125

Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
      130             135             140

```

<210> 484

<211> 30

<212> PRT

<213> Homo Sapien

<400> 484

```

Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
  1              5              10              15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
      20              25              30

```

<210> 485

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 485

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31

<210> 486

<211> 27

<212> DNA

<213> Artificial Sequence

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<223> Made in a lab

<400> 486

gcgaattctc acgctgagta tttggcc

27

<210> 487

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 487

cccgaattct tagctgcca tccgaacgcc ttcac

36

<210> 488

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 488

gggaagcttc ttccccggct gcaccagctg tgc

33

<210> 489

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 489

Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala  
1 5 10 15  
Ser Val Ala

<210> 490

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 490

Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys  
1 5 10 15  
Leu Ser His Ser  
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<210> 491

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 491

Thr	Cys	Leu	Ser	His	Ser	Val	Ala	Val	Val	Thr	Ala	Ser	Ala	Ala	Leu
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Thr	Gly	Phe	Thr												
				20											

<210> 492

<211> 20

<212> PRT

<213> Artificial Sequence

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<223> Made in a lab

<400> 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
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Leu	Ala	Ser	Leu												
				20											

<210> 493

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
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Lys	Tyr	Arg	Gly												
				20											

<210> 494

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
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Leu	Met	Ile	Ser												
				20											

<210> 495

<211> 20

<212> PRT

<213> Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 495

Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro  
1 5 10 15  
Phe Pro Asn Gly  
20

&lt;210&gt; 496

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 496

Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu  
1 5 10 15  
Pro Pro Pro Pro Ala  
20

&lt;210&gt; 497

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 497

Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val  
1 5 10 15  
Ser Val Arg Val  
20

&lt;210&gt; 498

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 498

Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val  
1 5 10 15  
Val Pro Gly Arg  
20

&lt;210&gt; 499

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

<213> Homo Sapiens

<220>

<221> misc\_feature

<222> (1)...(379)

<223> n = A,T,C or G

<400> 503

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<210> 504

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 504

Gly	Phe	Thr	Asn	Tyr	Thr	Asp	Phe	Glu	Asp	Ser	Pro	Tyr	Phe	Lys	Glu
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Asn	Ser	Ala													

<210> 505

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Made in a lab

<400> 505

Lys	Glu	Asn	Ser	Ala	Phe	Pro	Pro	Phe	Cys	Cys	Asn	Asp	Asn	Val	Thr
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Asn	Thr	Ala	Asn												
				20											

<210> 506

<211> 407

<212> DNA

<213> Homo Sapien

<400> 506

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<210> 507  
 <211> 422  
 <212> DNA  
 <213> Homo Sapien

<400> 507  
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 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360  
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 aa 422

<210> 508  
 <211> 411  
 <212> DNA  
 <213> Homo Sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(411)  
 <223> n = A,T,C or G

<400> 508  
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 cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360  
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<210> 509  
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 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 509  
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<210> 510  
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<220>  
 <223> Made in a lab

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 1 5 10 15

<210> 511  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 511

Tyr	His	Pro	Ser	Met	Phe	Cys	Ala	Gly	Gly	Gly	Gln	Asp	Gln	Lys
1				5				10					15	

<210> 512  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 512

Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu
1				5				10					15	

<210> 513  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 513

Ala	Pro	Cys	Gly	Gln	Val	Gly	Val	Pro	Asx	Val	Tyr	Thr	Asn	Leu
1				5				10					15	

<210> 514  
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<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 514

Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Ala	Ser
1				5				10					15	

<210> 515  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 515  
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1 5 10 15

<210> 516  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 516  
Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln  
1 5 10 15

<210> 517  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 517  
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1 5 10 15

<210> 518  
<211> 15  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Made in a lab

<400> 518  
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1 5 10 15

<210> 519  
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<212> PRT  
<213> Artificial Sequence

<220>  
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<400> 519  
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1 5 10 15  
Gly

<210> 520  
<211> 25  
<212> PRT  
<213> Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 520

Val	Gly	Glu	Gly	Leu	Tyr	Gln	Gly	Val	Pro	Arg	Ala	Glu	Pro	Gly	Thr
1				5				10						15	
Glu	Ala	Arg	Arg	His	Tyr	Asp	Glu	Gly							
			20				25								

&lt;210&gt; 521

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 521

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

&lt;210&gt; 522

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 522

Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys	Asp	Tyr	Gly	Ser	Gln	Glu	Asp
1				5					10					15	
Phe	Thr	Gln	Val												
			20												

&lt;210&gt; 523

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(254)

&lt;223&gt; Xaa = any amino acid

&lt;400&gt; 523

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5				10						15	
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
			20				25				30				
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
		35				40					45				

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Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
  50          55          60
Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
  65          70          75          80
Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
          85          90          95
Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
          100          105          110
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
          115          120          125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
          130          135          140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
  145          150          155          160
Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
          165          170          175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
          180          185          190
Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly
          195          200          205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
  210          215          220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
  225          230          235          240
Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
          245          250

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&lt;210&gt; 524

&lt;211&gt; 765

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 524

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tcgcagccct ggtagggcgc actgggtcatg gaaaacgaat tggtctgtctc gggcgctcctg      180
gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg      240
ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc      300
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atgcctaccg tgctgcagtg cgtgaacgtg tcgggtggtg ctgaggaggt ctgcagtaag      540
ctctatgacc cgctgtacca ccccagcatg ttctgcgccg gcggagggca agaccagaag      600
gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt      660
gtgtctttcg gaaaagcccc gtgtggccaa gttggcgtgc caggtgtcta caccaacctc      720
tgcaaatcca ctgagtggat agagaaaacc gtccaggcca gtttaa      765

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&lt;210&gt; 525

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 525

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Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
  1          5          10          15
Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
          20          25          30
Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu

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<210> 526
<211> 963
<212> DNA
<213> Homo sapiens
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<210> 527
<211> 320
<212> PRT
<213> Homo sapiens
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<400> 527

Met Ser Ser Cys Asn Phe Thr His Ala Thr Phe Val Leu Ile Gly Ile  
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 Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser  
                     20                    25                    30  
 Met Tyr Val Val Ala Met Phe Gly Asn Cys Ile Val Val Phe Ile Val  
                     35                    40                    45  
 Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met  
                     50                    55                    60  
 Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile  
                     65                    70                    75                    80  
 Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Phe Glu Ala Cys  
                     85                    90                    95  
 Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr  
                     100                    105                    110  
 Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro  
                     115                    120                    125  
 Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly  
                     130                    135                    140  
 Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu  
                     145                    150                    155                    160  
 Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser  
                     165                    170                    175  
 Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu  
                     180                    185                    190  
 Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val  
                     195                    200                    205  
 Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val  
                     210                    215                    220  
 Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys  
                     225                    230                    235                    240  
 Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly  
                     245                    250                    255  
 Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg  
                     260                    265                    270  
 Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro  
                     275                    280                    285  
 Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala  
                     290                    295                    300  
 Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys

305 310 315 320

<210> 528  
<211> 20  
<212> DNA  
<213> Homo Sapien

<400> 528  
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<210> 529  
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<213> Homo Sapien

<400> 529  
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<210> 530  
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<212> DNA  
<213> Homo sapiens

<400> 530  
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<210> 531  
<211> 879



<212> DNA

<213> Homo sapiens

<400> 531

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<210> 532

<211> 292

<212> PRT

<213> Homo sapiens

<400> 532

Met His Leu Ser Phe Pro Ala Phe Leu Pro Pro Trp Met Asp Arg Gly  
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Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp His Asn Asp Ser Ser  
20 25 30

Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe  
35 40 45

Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp  
50 55 60

Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu  
65 70 75 80

Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg  
85 90 95

Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp  
100 105 110

Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser  
115 120 125

Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu  
130 135 140

Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu  
145 150 155 160

Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile  
165 170 175

Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu  
 180 185 190

Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu  
 195 200 205

Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu  
 210 215 220

Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu  
 225 230 235 240

Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys  
 245 250 255

Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp  
 260 265 270

Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu  
 275 280 285

Val Ile Ile Met  
 290

<210> 533  
 <211> 801  
 <212> DNA  
 <213> Homo sapiens

<400> 533  
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 <211> 266  
 <212> PRT  
 <213> Homo sapiens

<400> 534  
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Arg Lys Gln Ala Ala Gly Ser Gly Ala Gly Tyr Ala Leu Pro Ser Ala  
 20 25 30

Leu Gln Ser Met Pro Gln Gly Ser Tyr Ala Thr Ala Arg Phe Leu Val  
 35 40 45

Ala Lys Arg Pro Thr Thr Gly His Leu Glu Lys Glu Phe Met Phe His  
 50 55 60

Cys Arg Lys Gln Pro Gly Ser Pro Ser Arg Gly Leu Gly Leu Leu Trp  
 65 70 75 80

Pro Trp Pro Asp Ile Glu Phe Val Pro Arg Gln Asp Lys Leu Thr Gln  
 85 90 95

Ser Ser Val Leu Val Pro Gln Ile Cys Ala Cys Gln Thr Arg Pro Asn  
 100 105 110

Trp Leu Asn Glu Gln Pro Ala Thr Ser Ala Gly Val Arg Leu Glu Glu  
 115 120 125

Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys  
 130 135 140

Ser His Ser Leu Ser Gly Cys His Leu Met Ala Asp Ile Ala Lys Ala  
 145 150 155 160

Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr  
 165 170 175

Asp Val Pro Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser  
 180 185 190

Ser Trp His Thr Leu Ala Glu Val Thr Gly Cys Ser Leu Ser Pro Leu  
 195 200 205

Ser Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys  
 210 215 220

Trp Ser His Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr  
 225 230 235 240

Ala Ala Phe Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu  
 245 250 255

Trp Ala Ser Trp Leu Pro Arg Gly Arg Pro  
 260 265

<210> 535

<211> 6082

<212> DNA

<213> Homo sapiens

<400> 535

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	145		150			155
						160
Cys Ala Gly Met	Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg					
	165		170			175
Lys Ala Leu Arg	Leu Ser Asn Met Ala Met Gly Lys Thr Thr Thr Gly					
	180		185			190
Gln Ile Val Asn	Leu Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val					
	195		200			205
Thr Val Phe Leu	His Phe Leu Trp Ala Gly Pro Leu Gln Ala Ile Ala					
	210		215			220
Val Thr Ala Leu	Leu Trp Met Glu Ile Gly Ile Ser Cys Leu Ala Gly					
	225		230			235
						240
Met Ala Val Leu	Ile Ile Leu Leu Pro Leu Gln Ser Cys Phe Gly Lys					
	245		250			255
Leu Phe Ser Ser	Leu Arg Ser Lys Thr Ala Thr Phe Thr Asp Ala Arg					
	260		265			270
Ile Arg Thr Met	Asn Glu Val Ile Thr Gly Ile Arg Ile Ile Lys Met					
	275		280			285
Tyr Ala Trp Glu	Lys Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys					
	290		295			300
Lys Glu Ile Ser	Lys Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn					
	305		310			315
						320
Leu Ala Ser Phe	Phe Ser Ala Ser Lys Ile Ile Val Phe Val Thr Phe					
	325		330			335
Thr Thr Tyr Val	Leu Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe					
	340		345			350
Val Ala Val Thr	Leu Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe					
	355		360			365
Phe Pro Ser Ala	Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg					
	370		375			380



Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg  
 385 390 395 400  
 Gln Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr  
 405 410 415  
 Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser  
 420 425 430  
 Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly  
 435 440 445  
 Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro  
 450 455 460  
 Ser His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln  
 465 470 475 480  
 Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly  
 485 490 495  
 Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala  
 500 505 510  
 Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile  
 515 520 525  
 Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn  
 530 535 540  
 Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp  
 545 550 555 560  
 Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu  
 565 570 575  
 Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His  
 580 585 590  
 Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp  
 595 600 605  
 Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly  
 610 615 620  
 Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln  
 625 630 635 640  
 Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu  
 645 650 655  
 Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly  
 660 665 670  
 Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu  
 675 680 685

Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr  
 690 695 700  
 Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Leu  
 705 710 715 720  
 Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln Asp Trp Trp Leu Ser  
 725 730 735  
 Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val Thr Val Asn Gly Gly  
 740 745 750  
 Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp Tyr Leu Gly Ile Tyr  
 755 760 765  
 Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly Ile Ala Arg Ser Leu  
 770 775 780  
 Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln Thr Leu His Asn Lys  
 785 790 795 800  
 Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu Phe Phe Asp Arg Asn  
 805 810 815  
 Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys Asp Ile Gly His Leu  
 820 825 830  
 Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe Ile Gln Thr Leu Leu  
 835 840 845  
 Gln Val Val Gly Val Val Ser Val Ala Val Ala Val Ile Pro Trp Ile  
 850 855 860  
 Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe Ile Phe Leu Arg Arg  
 865 870 875 880  
 Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg Leu Glu Ser Thr Thr  
 885 890 895  
 Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser Leu Gln Gly Leu Trp  
 900 905 910  
 Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys Gln Glu Leu Phe Asp  
 915 920 925  
 Ala His Gln Asp Leu His Ser Glu Ala Trp Phe Leu Phe Leu Thr Thr  
 930 935 940  
 Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile Cys Ala Met Phe Val  
 945 950 955 960  
 Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala Lys Thr Leu Asp Ala  
 965 970 975  
 Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu Thr Leu Met Gly Met  
 980 985 990  
 Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val Glu Asn Met Met Ile

995	1000	1005
Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu Glu Lys Glu Ala Pro 1010 1015 1020		
Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp Pro His Glu Gly Val 1025 1030 1035 1040		
Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser Pro Gly Gly Pro Leu 1045 1050 1055		
Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser Gln Glu Lys Val Gly 1060 1065 1070		
Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Ile Ser Ala Leu 1075 1080 1085		
Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp Ile Asp Lys Ile Leu 1090 1095 1100		
Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile 1105 1110 1115 1120		
Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp 1125 1130 1135		
Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu 1140 1145 1150		
Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr 1155 1160 1165		
Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu 1170 1175 1180		
Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile 1185 1190 1195 1200		
Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr Asp Glu Leu Ile Gln 1205 1210 1215		
Lys Lys Ser Gly Arg Asn Leu Pro Thr Ala Pro Cys 1220 1225		
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Leu Gln Gly Phe Trp Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala 20 25 30		
Gln Lys Pro Ser Leu Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser 35 40 45		

Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val  
 50 55 60  
 Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr  
 65 70 75 80  
 Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr  
 85 90 95  
 Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr  
 100 105 110  
 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys  
 115 120 125  
 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly  
 130 135 140  
 Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn  
 145 150 155 160  
 Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro  
 165 170 175  
 Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile  
 180 185 190  
 Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln  
 195 200 205  
 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr  
 210 215 220  
 Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile  
 225 230 235 240  
 Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile  
 245 250 255  
 Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys  
 260 265 270  
 Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile  
 275 280 285  
 Val Phe Val Thr Phe Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr  
 290 295 300  
 Ala Ser Arg Val Phe Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu  
 305 310 315 320  
 Thr Val Thr Leu Phe Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala  
 325 330 335  
 Ile Val Ser Ile Arg Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile  
 340 345 350

Ser Gln Arg Asn Arg Gln Leu Pro Ser Asp Gly Lys Lys Met Val His  
 355 360 365  
 Val Gln Asp Phe Thr Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr  
 370 375 380  
 Leu Gln Gly Leu Ser Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val  
 385 390 395 400  
 Val Gly Pro Val Gly Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu  
 405 410 415  
 Gly Glu Leu Ala Pro Ser His Gly Leu Val Ser Val His Gly Arg Ile  
 420 425 430  
 Ala Tyr Val Ser Gln Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser  
 435 440 445  
 Asn Ile Leu Phe Gly Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val  
 450 455 460  
 Ile Lys Ala Cys Ala Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly  
 465 470 475 480  
 Asp Leu Thr Val Ile Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln  
 485 490 495  
 Lys Ala Arg Val Asn Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile  
 500 505 510  
 Tyr Leu Leu Asp Asp Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg  
 515 520 525  
 His Leu Phe Glu Leu Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr  
 530 535 540  
 Ile Leu Val Thr His Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile  
 545 550 555 560  
 Leu Ile Leu Lys Asp Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu  
 565 570 575  
 Phe Leu Lys Ser Gly Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn  
 580 585 590  
 Glu Glu Ser Glu Gln Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn  
 595 600 605  
 Arg Thr Phe Ser Glu Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro  
 610 615 620  
 Ser Leu Lys Asp Gly Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro  
 625 630 635 640  
 Val Thr Leu Ser Glu Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln  
 645 650 655  
 Ala Tyr Lys Asn Tyr Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile

660					665					670						
Phe	Leu	Ile	Leu	Leu	Asn	Thr	Ala	Ala	Gln	Val	Ala	Tyr	Val	Leu	Gln	
675					680					685						
Asp	Trp	Trp	Leu	Ser	Tyr	Trp	Ala	Asn	Lys	Gln	Ser	Met	Leu	Asn	Val	
690					695					700						
Thr	Val	Asn	Gly	Gly	Gly	Asn	Val	Thr	Glu	Lys	Leu	Asp	Leu	Asn	Trp	
705					710					715					720	
Tyr	Leu	Gly	Ile	Tyr	Ser	Gly	Leu	Thr	Val	Ala	Thr	Val	Leu	Phe	Gly	
725					730					735						
Ile	Ala	Arg	Ser	Leu	Leu	Val	Phe	Tyr	Val	Leu	Val	Asn	Ser	Ser	Gln	
740					745					750						
Thr	Leu	His	Asn	Lys	Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu	
755					760					765						
Phe	Phe	Asp	Arg	Asn	Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys	
770					775					780						
Asp	Ile	Gly	His	Leu	Asp	Asp	Leu	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe	
785					790					795					800	
Ile	Gln	Thr	Leu	Leu	Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala	
805					810					815						
Val	Ile	Pro	Trp	Ile	Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe	
820					825					830						
Ile	Phe	Leu	Arg	Arg	Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg	
835					840					845						
Leu	Glu	Ser	Thr	Thr	Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser	
850					855					860						
Leu	Gln	Gly	Leu	Trp	Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys	
865					870					875					880	
Gln	Glu	Leu	Phe	Asp	Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe	
885					890					895						
Leu	Phe	Leu	Thr	Thr	Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile	
900					905					910						
Cys	Ala	Met	Phe	Val	Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala	
915					920					925						
Lys	Thr	Leu	Asp	Ala	Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu	
930					935					940						
Thr	Leu	Met	Gly	Met	Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val	
945					950					955					960	
Glu	Asn	Met	Met	Ile	Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu	
965					970					975						

Glu Lys Glu Ala Pro Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp  
 980 985 990  
 Pro His Glu Gly Val Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser  
 995 1000 1005  
 Pro Gly Gly Pro Leu Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser  
 1010 1015 1020  
 Gln Glu Lys Val Gly Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser  
 1025 1030 1035 1040  
 Leu Ile Ser Ala Leu Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp  
 1045 1050 1055  
 Ile Asp Lys Ile Leu Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys  
 1060 1065 1070  
 Lys Met Ser Ile Ile Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met  
 1075 1080 1085  
 Arg Lys Asn Leu Asp Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp  
 1090 1095 1100  
 Asn Ala Leu Gln Glu Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro  
 1105 1110 1115 1120  
 Gly Lys Met Asp Thr Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val  
 1125 1130 1135  
 Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn  
 1140 1145 1150  
 Gln Ile Leu Ile Ile Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr  
 1155 1160 1165  
 Asp Glu Leu Ile Gln Lys Lys Ile Arg Glu Lys Phe Ala His Cys Thr  
 1170 1175 1180  
 Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys  
 1185 1190 1195 1200  
 Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr  
 1205 1210 1215  
 Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln  
 1220 1225 1230  
 Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg  
 1235 1240 1245  
 Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser  
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Cys Leu Ser His Ser Val Ala Val Val Thr  
1 5 10

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<220>

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Ala Val Val Thr Ala Ser Ala Ala Leu  
1 5

<210> 541

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<400> 541

Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu  
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<210> 542

<211> 15

<212> PRT

<213> Homo sapiens

<400> 542

Thr Gln Val Val Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
5 10 15

<210> 543

<211> 12

<212> PRT

<213> Homo sapiens

<400> 543

Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val  
5 10

<210> 544

<211> 18

<212> PRT

<213> Homo sapiens

<400> 544

Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe



5

10

15

Met Thr

&lt;210&gt; 545

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 545

Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala  
                                   5                                  10                                  15

Ser Val

&lt;210&gt; 546

&lt;211&gt; 29

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 546

Phe Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly  
                                   5                                  10                                  15

Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met  
                                   20                                  25

&lt;210&gt; 547

&lt;211&gt; 58

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 547

Val Ala Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu  
                                   5                                  10                                  15

Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu  
                                   20                                  25                                  30

Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys  
                                   35                                  40                                  45

Cys Arg Met Pro Arg Thr Leu Arg Arg Leu  
                                   50                                  55

&lt;210&gt; 548

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 548

Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu

200

5

10

15

Glu Cys

&lt;210&gt; 549

&lt;211&gt; 18

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 549

Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg  
5 10 15

Gln Ala

&lt;210&gt; 550

&lt;211&gt; 14

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 550

Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe  
5 10

&lt;210&gt; 551

&lt;211&gt; 11

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 551

Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
1 5 10